Supplemental Table 1: Absolute difference (95% confidence Interval) in 3, 4, and 5 years rates of outcomes between 3 months and 6 months of therapy with 6 months group as reference group

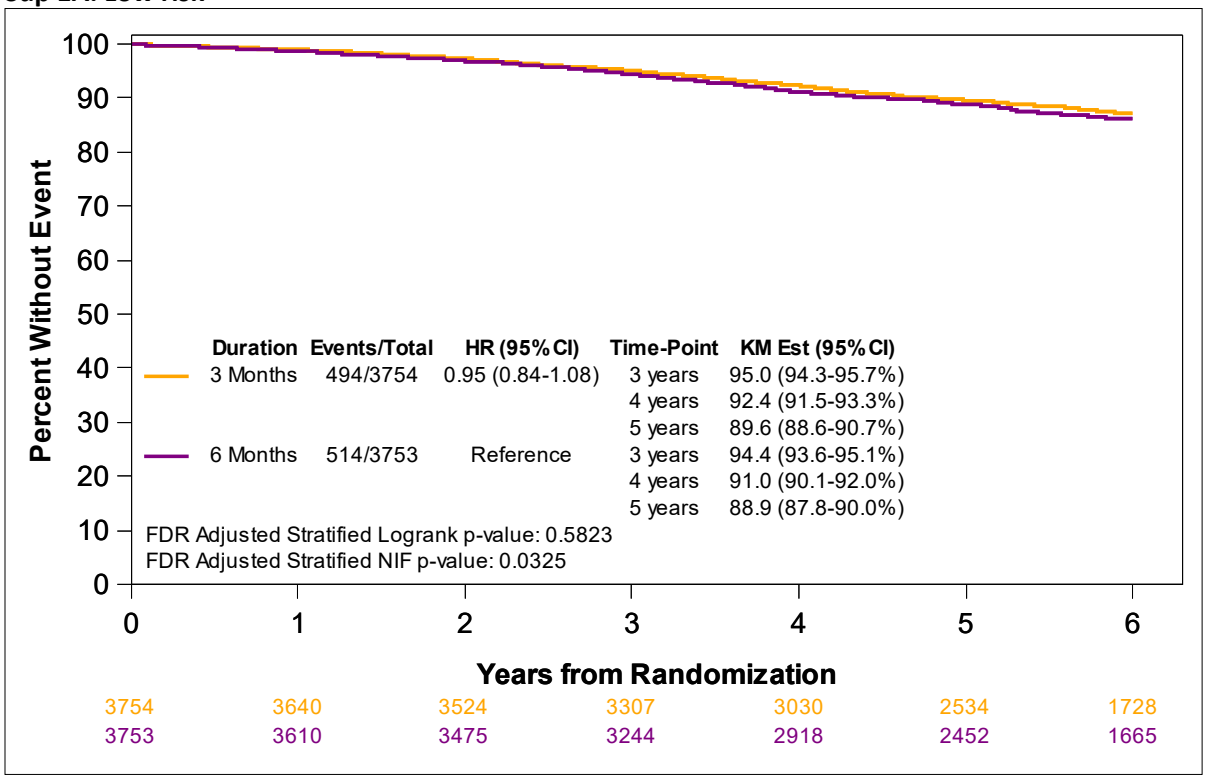
Cohort	3-year Rate Difference	4-year Rate Difference	5-year Rate Difference
Disease-free Survival			
Overall	-0.9% (-2.8 to 1.0%)	-1.7% (-3.9 to 0.5%)	-1.7% (-4.2 to 0.8%)
Overall Survival			
Overall	0.6% (-0.5 to 1.7%)	0.6% (-0.8 to 2.0%)	-0.4% (-2.1 to 1.3%)
CAPOX	1.1% (-0.7 to 2.9%)	1.6% (-0.7 to 3.9%)	0.9% (-1.8 to 3.6%)
FOLFOX	0.3% (-1.1 to 1.7%)	0.0% (-1.8 to 1.8%)	-1.2% (-3.3 to 0.9%)
Low Risk	0.6% (-0.5 to 1.7%)	1.4% (0.0 to 2.8%)	0.7% (-1.0 to 2.4%)
High Risk	0.6% (-1.6 to 2.8%)	-0.4 (-3.1 to 2.3%)	-2.1% (-5.3 to 1.1%)

Supplemental Table 2: Comparing outcomes between 3 vs. 6 months of therapy by regimen in individual trials

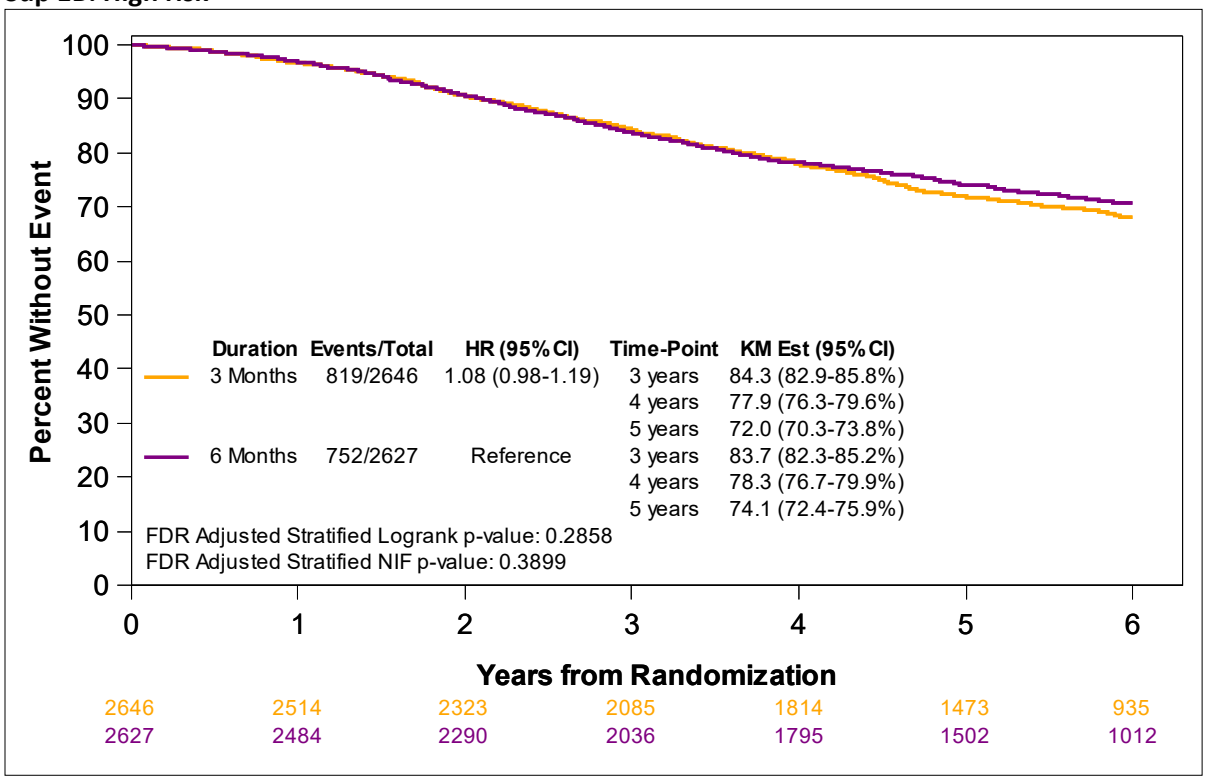
		OS				DFS			
Study	**Duration**	**N of events / N of patients**	**5-year rate (95% CI)**	**Absolute difference (95% CI)**	**HR (95% CI)**	**N of events / N of patients**	**5-year rate (95% CI)**	**Absolute difference (95% CI)**	**HR (95% CI)**
CAPOX (Studies with sample size >500)									
TOSCA	3m	78/419	85.0 (81.0-88.3%)	1.8 (-4.5, 8.1%)	0.96 (0.70-1.31)	117/419	71.4 (66.4-75.8%)	-0.3 (-10.3, 9.7%)	1.01 (0.78-1.30)
	6m	81/414	83.2 (79.0-86.7%)	--	--	117/414	71.7 (66.6-76.1%)	--	--
SCOT	3m	318/1330	79.0 (76.6-81.2%)	0.6 (-3.3, 4.5%)	0.95 (0.82-1.11)	417/1330	66.2 (63.2-69.1%)	0.9 (-5.6, 7.4%)	0.96 (0.84-1.10)
	6m	326/1319	78.4 (75.9-80.6%)	--	--	432/1319	65.3 (62.3-68.1%)	--	--
ACHIEVE	3m	57/487	88.3 (85.1-90.9%)	1.1 (-4.0, 6.2%)	0.87 (0.61-1.24)	109/487	77.2 (73.2-80.7%)	1.2 (-6.7, 9.1%)	0.93 (0.72-1.21)
	6m	63/482	87.2 (83.8-90.0%)	--	--	114/482	76.0 (71.8-79.6%)	--	--
FOLFOX (Studies with sample size >500)									
C80702	3m	206/1240	82.9 (80.5-85.1%)	0.2 (-4.0, 4.4%)	0.94 (0.78-1.14)	364/1240	67.3 (64.3-70.2%)	-2.6 (-9.6, 4.4%)	1.13 (0.97-1.31)
	6m	208/1212	82.7 (80.2-84.9%)	--	--	312/1212	69.9 (66.9-72.8%)	--	--
IDEA France	3m	187/895	83.5 (80.9-85.9%)	-3.1 (-7.0, 0.8%)	1.21 (0.98-1.49)	304/895	67.9 (64.7-70.9%)	-4.8 (-10.5, 0.9%)	1.27 (1.07-1.50)
	6m	161/914	86.6 (84.1-88.7%)	--	--	254/914	72.7 (69.6-75.5%)	--	--
TOSCA	3m	176/768	83.2 (80.3-85.8%)	-0.7 (-5.2, 3.8%)	1.09 (0.88-1.35)	236/768	71.2 (67.7-74.4%)	-2.9 (-9.0, 3.2%)	1.13 (0.94-1.36)
	6m	163/790	83.9 (81.0-86.4%)	--	--	217/790	74.1 (70.8-77.1%)	--	--
SCOT	3m	151/662	80.0 (76.5-83.0%)	-2.5 (-7.8, 2.8%)	1.18 (0.93-1.49)	208/662	65.5 (61.0-69.7%)	-5.7 (-15.0, 3.6%)	1.22 (1.00-1.49)
	6m	131/672	82.5 (79.3-85.3%)	--	--	178/672	71.2 (66.9-75.0%)	--	--

Supplemental Figure 1: Overall survival with 3 months versus 6 months of adjuvant therapy by risk groups

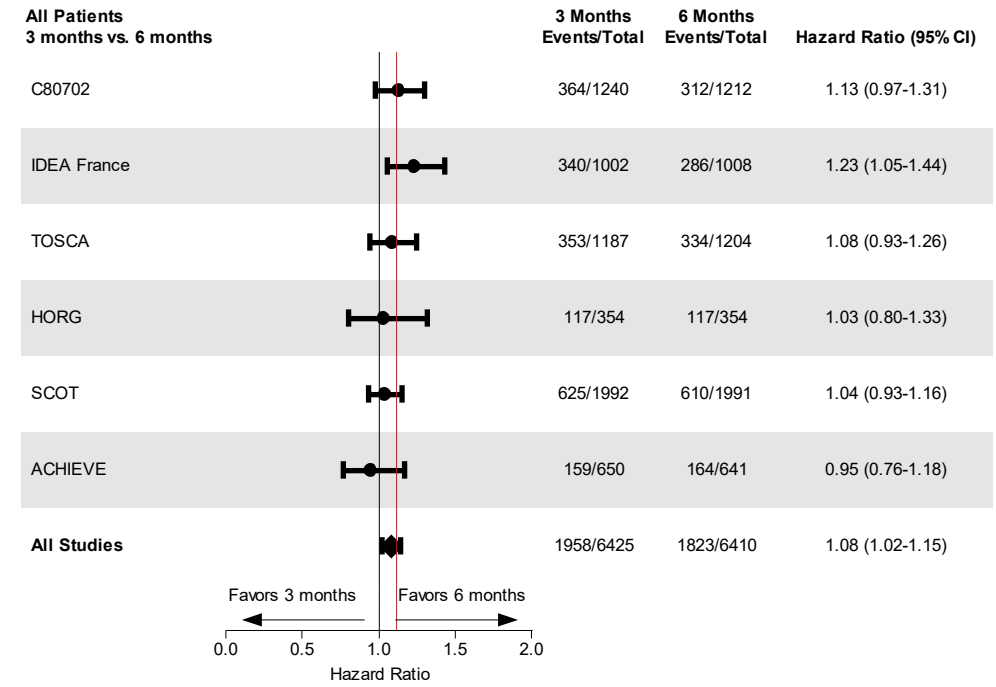
Sup 1A: Low risk



Sup 1B: High risk

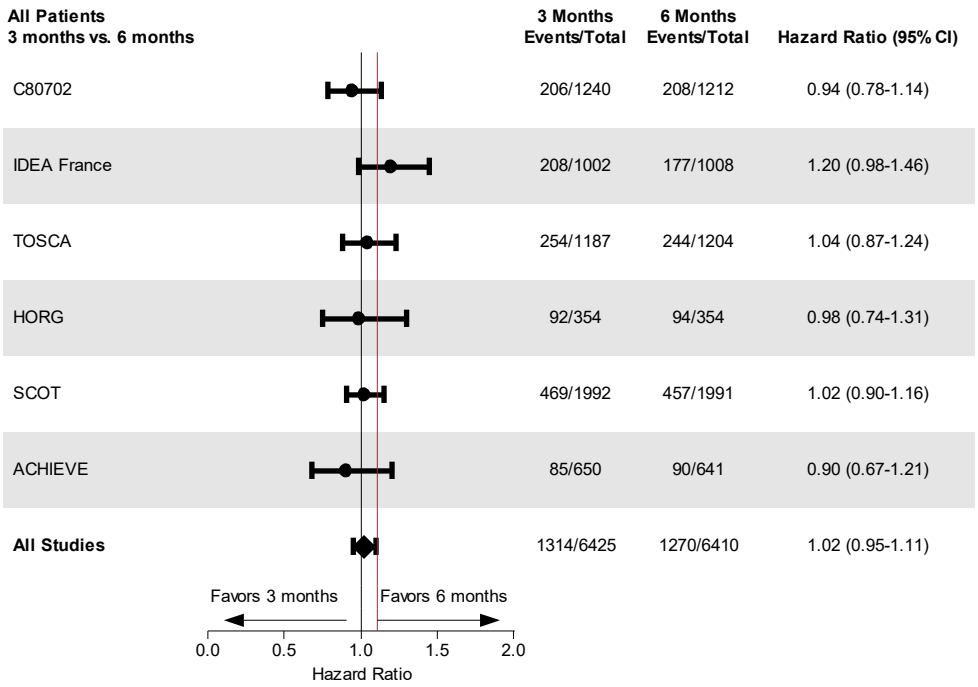


Supplemental Figure 2: Comparing outcomes between 3 vs. 6 months of therapy in individual trials
Sup 2A: Disease-free survival



Q-statistic (p-value)=5.105 (0.4032)
I^2: 2.0601

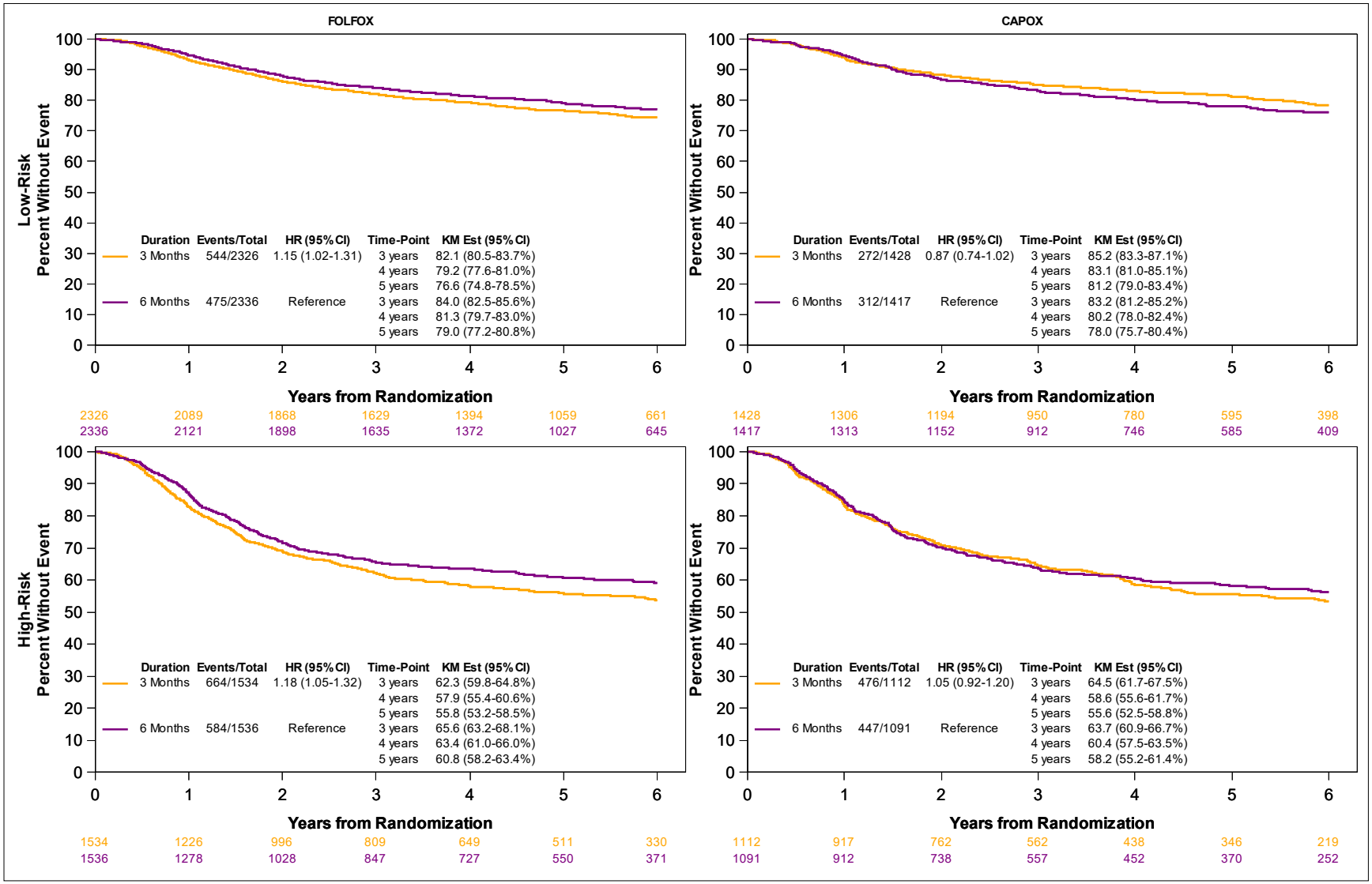
Sup 2B: Overall survival



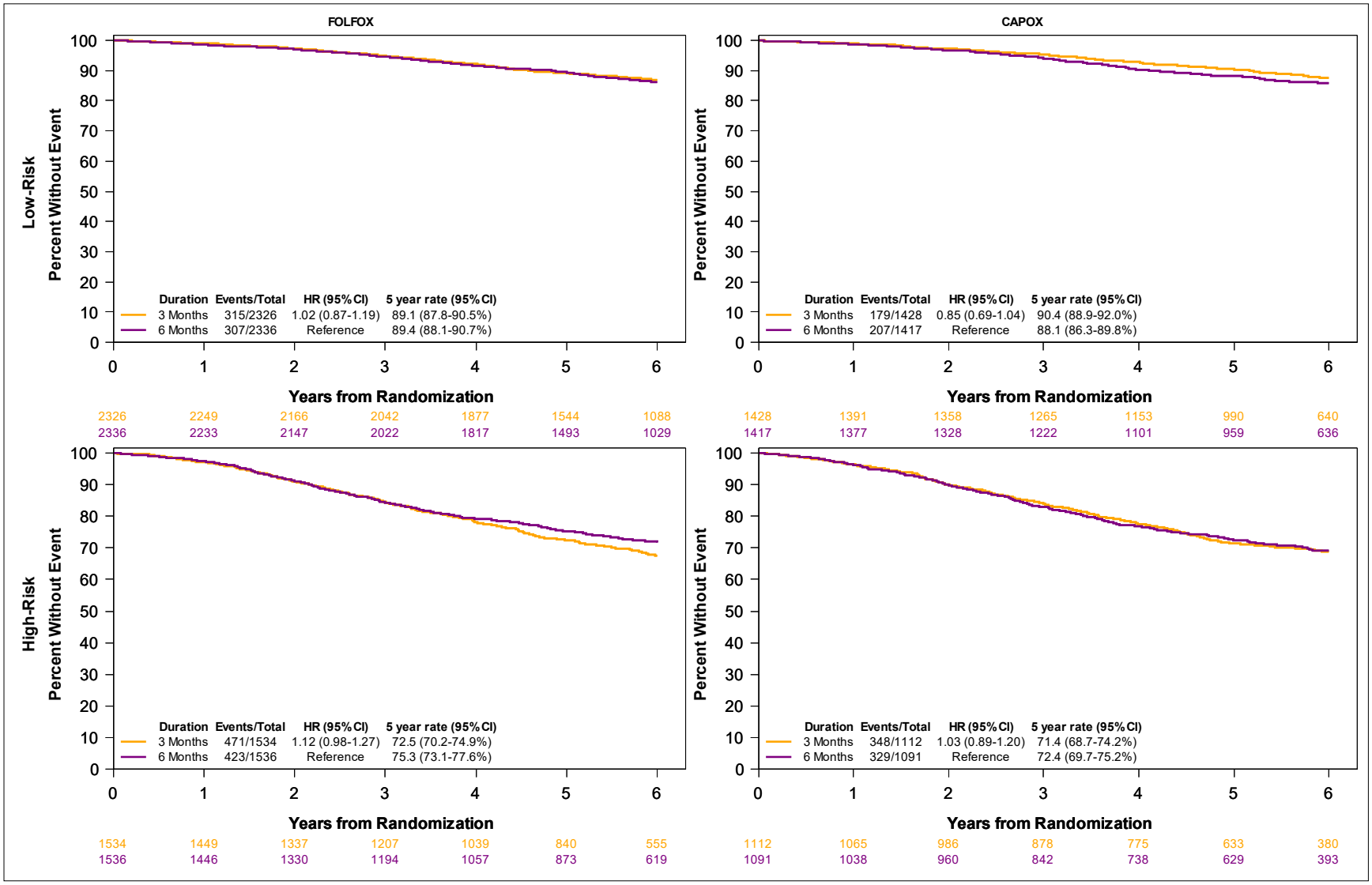
Q-statistic (p-value)=3.823 (0.5751)
I^2: 0.0000

Supplemental Figure 3: Comparing overall survival and disease free survival between 3 months versus 6 months of adjuvant therapy in subgroups defined by combinations of regimen and risk groups

3A: Disease-free survival

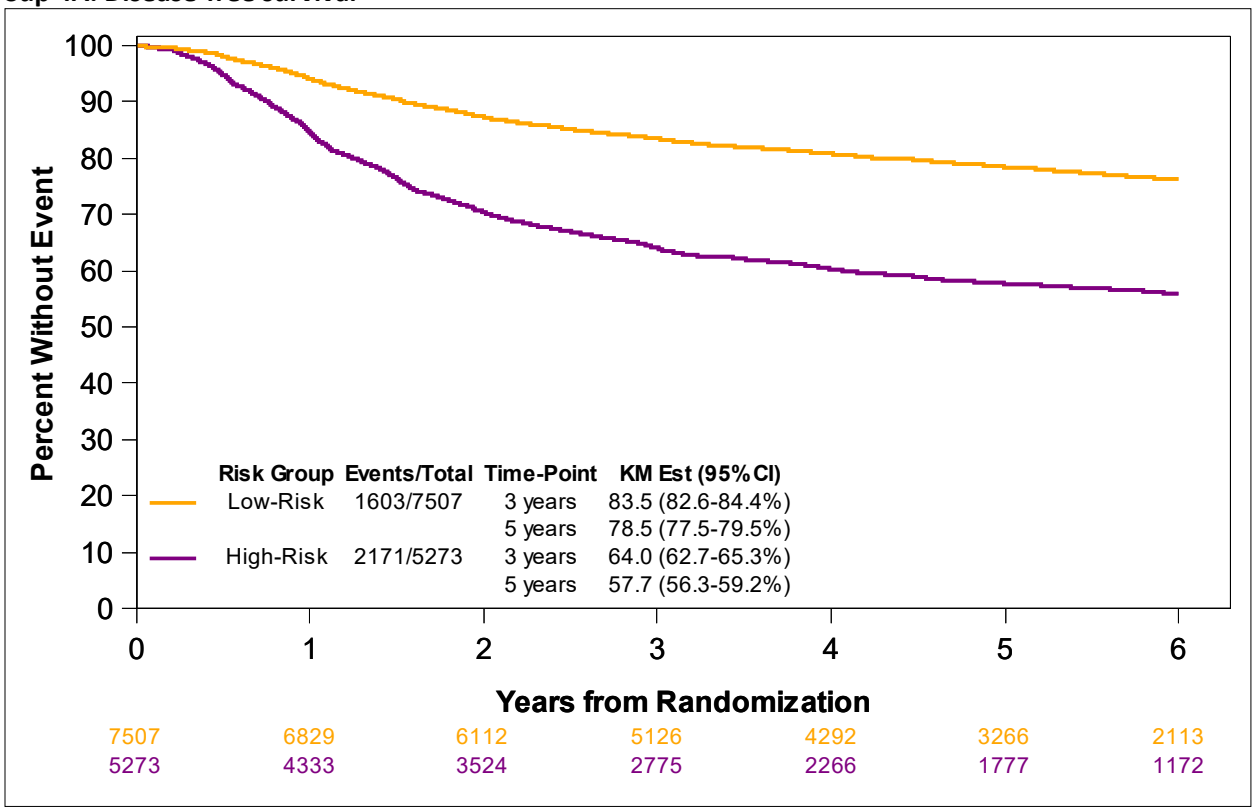


3B: Overall survival

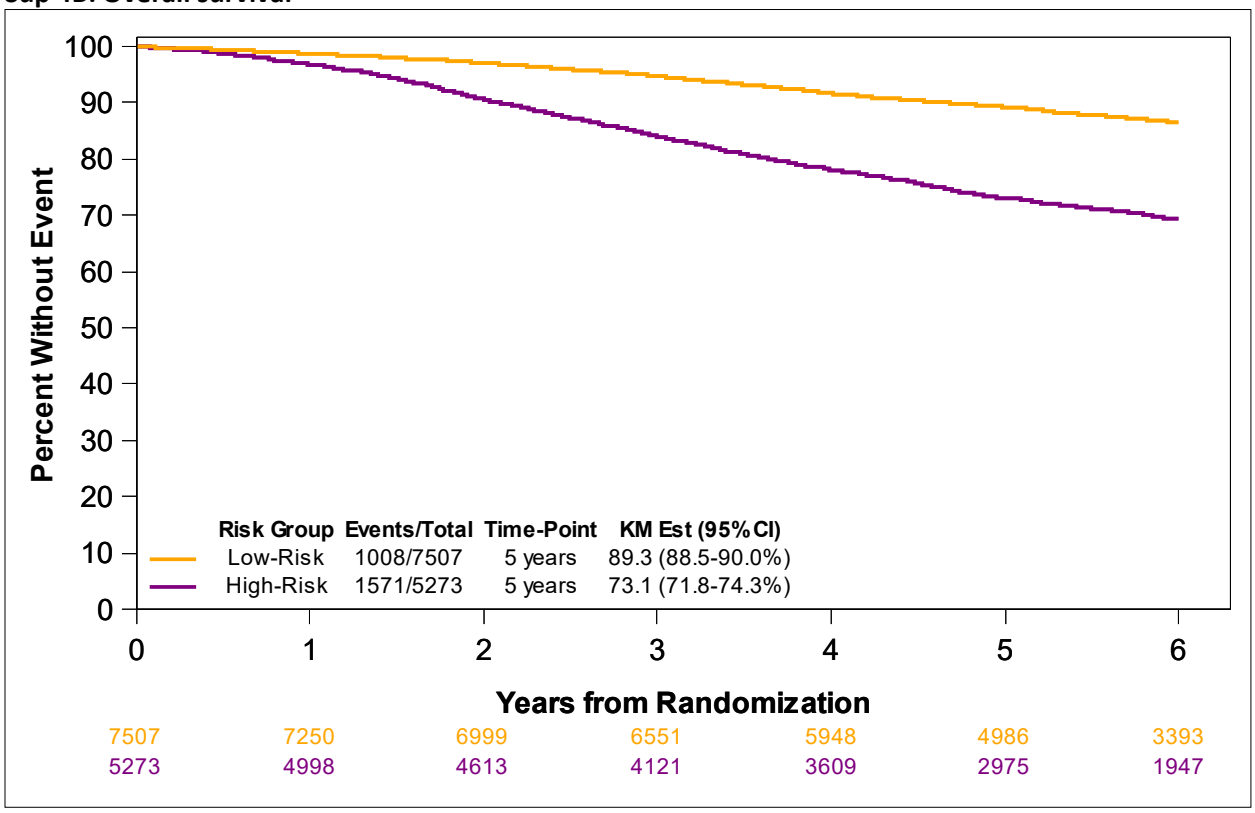


Supplemental Figure 4: Comparing overall survival and disease free survival between risk groups

Sup 4A: Disease-free survival



Sup 4B: Overall survival



STATISTICAL ANALYSIS PLAN

Prospective Combined Analysis of Phase III Trials Investigating Duration of Adjuvant Therapy with the FOLFOX (FOLFOX4 or Modified FOLFOX6) or CAPOX (3 versus 6 months) Regimen for Patients with Stage III Colon Cancer – Overall Survival, Updated Disease-free Survival Analyses, and Pre-Planned Exploratory Analyses

DATE: Oct 15, 2019
Version: 1.1

Prepared by:

IDEA SDC: Qian Shi, PhD,
IDEA: Axel Grothey, MD
TOSCA (GISCAD): Fabio Galli, PhD, Roberto Labianca, MD, Alberto Sobrero, MD
SCOT (CACTUS/OCTO): Caroline Kelly, MSc, Timothy Iveson, MD
IDEA France (PRODIGE/GERCOR): Thierry Andre, MD, Julien Taieb MD
C80702 (CALGB/SWOG): Qian Shi, PhD, Jeffrey Meyerhardt, MD, MPH, Anthony Shields, MD. PhD
HORG (HORG): Ioannis Souglakos, MD
ACHIEVE (JFMC): Takeharu Yamanaka, PhD, Takayuki Yoshino, MD

TABLE OF CONTENTS

1. INTRODUCTION AND OBJECTIVES

Previously the International Duration Evaluation of Adjuvant Therapy (IDEA) collaboration conducted the prospectively planned pooled analyses of individual patient data from six randomized, multicenter, clinical trials conducted around the world to test the hypothesis whether 3-month course of adjuvant therapy (FOLFOX4/mFOLFOX6 or CAPOX) is non-inferior to the current standard of 6-month treatment for patients with stage III colon cancer, regarding the primary endpoint of disease-free survival (DFS). This primary DFS analyses were based on data frozen on Feb 1st, 2017. The results were reported at ASCO 2017 annual meeting and published in the New England Journal of Medicine.[1ref] The median follow-time ranged from 34.9 to 61.7 months across six trials.

It was anticipated that the median follow-time will reach 5 years or longer for all six trials by Dec of 2019. In this statistical analysis plan (SAP), we describe prospectively the statistical methods, analyses and data presentations to be used in the following analyses:

1. To evaluate the non-inferiority of 3-month course of adjuvant therapy (FOLFOX4/mFOLFOX6 or CAPOX), compared to 6-month treatment for patients with stage III colon cancer, for the **secondary endpoint of overall survival (OS)**, with pre-specified statistical hypothesis test.
2. To provide updated comparison between duration of treatments regarding the primary endpoint of disease-free survival (DFS) and estimations of DFS at 3 years, 4 years, and 5 years.
3. To conduct pre-planned exploratory analyses regarding the primary endpoint of DFS and secondary endpoint of OS.

This SAP was developed and approved by all individual trial investigators and statisticians before any formal analyses were conducted. All statistical analyses detailed in this SAP will be conducted using *SAS® Version 9.4 or validated statistical software*.

2. ANALYSIS POPULATION

Summary of six clinical trials see Grothey et al.

2.1. Primary Analyses Populations

The **non-inferiority hypothesis testing analyses** for **both primary endpoint of DFS and secondary endpoint of OS** will be conducted following modified intention to treat (**mITT**) principle: "*including patients in their randomized group, irrespective of the actual treatment or duration of treatment received, with only patients who received no therapy whatsoever excluded from the analysis*". [1]

The operational definition of mITT population is defined as the following:

Inclusion criteria:

- Randomized to duration treatments (i.e. 3m or 6m FOLFOX/CAPOX)
- Received any treatment of FOLFOX/CAPOX (i.e., dose of any of the agents > 0 mg)

Exclusion criteria:

- Did not receive any treatment of FOLFOX/CAPOX
- For the studies designed to enroll stage II and III patients (TOSCA, SCOT, and HORG), the patients deemed as stage II colon cancer at enrollment will be excluded
- For the studies designed to enroll colon and rectal cancer patients (SCOT), the patients deemed as rectal cancer at enrollment will be excluded

According to this definition, the following patients will be *included* in the mITT population for the primary analysis:

- For the studies designed to only enroll stage III patients (IDEA France, C80702, ACHIEVE), patients deemed as stage I, II or IV after randomization and received treatment
- For the studies designed to enroll both stage II and III patients (TOSCA, SCOT, and HORG), the patients registered as stage III patients, but were deemed as stage I, II or IV after randomization and received treatment
- Patients deemed ineligible after randomization and received any treatment due to any reasons other than stage classifications

Treatment grouping: All patients will be included in their randomized duration group (3 vs. 6 months), irrespective of the actual duration of the treatment received.

2.2. Sensitivity Analysis Populations

2.2.1. Strict ITT population

This population is defined as all patients who were deemed as stage III colon cancer at enrollment and randomized to duration groups, regardless of received any treatment or not. The patients will be included in their randomized duration group (3 vs. 6 months), irrespective of the actual duration of treatment received.

2.2.2. Per-protocol (PP) analysis population

All patients who fit the inclusion/exclusion criteria listed in section 3.2, and received the length of therapy specified as the following:

3m arm	**6m arm**
Completed all 3 months of treatment (i.e., 12 weeks*) **To avoid bias, all patients who had events (recurrence or death for DFS, death for OS) on treatment will be included in PP analysis population.**	Completed ≥ 5 months of treatment (i.e., 20 weeks*) **To avoid bias, all patients who had events (recurrence or death for DFS, death for OS) on treatment will be included in PP analysis population.**

*Calculation definition see section 5.3, item 1.

Exploratory analyses:

Comparisons between two duration groups according to the subgroups defined as in the following table:

3m arm	**6m arm**
Completed < 3 months of treatment	Completed < 3 months of treatment
Completed all 3 months of treatment (i.e., 12 weeks*)	Completed > 3 months of treatment (i.e., 12 weeks*)
Completed all 3 months of treatment (i.e., 12 weeks*)	Completed ≥ 4 months of treatment (i.e., 16 weeks*)
Completed all 3 months of treatment (i.e., 12 weeks*)	Completed ≥ 5 months of treatment (i.e., 20 weeks*)
Completed all 3 months of treatment (i.e., 12 weeks*)	Completed = 6 months of treatment (i.e., 24 weeks*)

Forest plot of HRs (95% CIs) will be used to summarize these results.

3. PRIMARY ENDPOINT

"*The primary efficacy endpoint for the IDEA combined analysis is disease-free survival (DFS) at three years, defined as the time from randomization to relapse or death, whichever occurred first. Secondary colorectal cancers are regarded as DFS events, whereas non-colorectal tumors are to be disregarded in the analysis*."[2]

Note: For the SCOT trial, the start date of DFS for patients who were randomized at 12 weeks will be the registration date.

3.1. Definition of events

	Recurrence		2nd primary colorectal cancer	Death related to colon cancer?	
	Local	Distant		Yes	No
DFS event Definition	Event	Event	Event	Event	Event

Event date will be the earliest date of all events observed.

3.2. Definition of censoring rules

- Patients with no defined events observed during the follow-up will be censored at the date of last disease evaluation which showed no evidence of relapse, or secondary primary colorectal cancer.
- The following table specifies the censoring rules for special cases:

Scenarios	**Status**	**Censoring/Event date**
No any defined events observed	Censor	Last disease evaluation
Data were not collected whatsoever	Censor	Day 1 after randomization date
No follow-up disease evaluation after starting treatment	Censor	last reported treatment date
Had mets at enrollment/randomization	Censor	Day 1 of the treatment
Mets detected after enrollment/ randomization	Event	Mets detection dates

4. SECONDARY ENDPOINT

The secondary endpoint is overall survival, defined as the time from randomization to death due to all causes. Note: For SCOT trial, the start date of DFS for patients who were randomized at 12 weeks will be the registration date

4.1. Definition of events

	Death related to colon cancer?	
	Yes	No
OS event Definition	Event	Event

4.2. Definition of censoring rules

- Patients with no defined events observed during the follow-up will be censored at the date of follow-up with last known alive status.
- The following table specifies the censoring rules for special cases:

Scenarios	**Status**	**Censoring/Event date**
No any defined events observed	Censor	Latest follow-up with known alive status
Data were not collected whatsoever	Censor	Day 1 after randomization date

5. STATISTICAL ANALYTIC METHODS AND CONSIDERATIONS

To avoid duplications in reporting between IDEA combined and individual trial publications, IDEA combined analyses will report aggregated results (pooling treatment groups or pooling studies) as much as possible and when it is appropriate. In case of substantial heterogeneity in treatment effects is detected across studies, individual study results may be presented. However, the consensus has to be reached among all steering committee members before any individual trial data disclosure.

5.1. Handling missing dates

For partial and missing dates, the following data management will only be performed for events (death, recurrence, 2nd colorectal primary tumor) related dates:

1. Missing event dates: If the event dates are all missing even at least one of the event indicators indicates that the event was observed, the patient will be censored at the last disease evaluation date, since the exact date is unknown
2. Partial dates:
    - If year and month are not missing, then the missing day value will be imputed with 1st day of the month
    - If either year or month is missing, the date will be treated as missing date, and the DFS time/censor will be calculated per item # 1 if applicable

5.2. Descriptive statistics of time-to-event endpoints

The follow-up by the reverse Kaplan-Meier method in the pooled population and in each individual studies will be reported.

The DFS and OS will be summarized by Kaplan-Meier estimates by treatment duration groups, combing all studies. DFS and OS rates at specific time points and 95% confidence interval (CI) will be estimated based on Kaplan-Meier curves.

5.3. Treatment comparison and treatment effect estimation

Stratified log-rank test, stratified by studies, will be used to compare time-to-event endpoints between treatment duration groups. For treatment effects, the hazard ratio (HR) and its two-sided 95% CI based on Cox model, stratified by study, will be reported. Adjusted HRs will be estimated based on multivariable (MV) stratified Cox regression model when it is applicable. Proportional hazard assumption will be evaluated by scaled Schoenfeld residuals methods (cox.zph function in R).

Difference in DFS/OS rates at specific time point, with standard error/two-sided 95% CI will be reported.

5.4. Assessing treatment effect heterogeneity

Individual trial HRs with confidence intervals will be plotted using a forest plot. Potential heterogeneity in treatment effects will be assessed by Q and I^2 statistics. If heterogeneity in the treatment effect across studies is detected, subgroup analysis (excluding outlier trial(s)) and meta-regression analysis will be conducted to assess the robustness of the primary efficacy results and investigate the trial characteristics (trial design, enrolling country, disease characteristic difference, etc.) which may contribute to the heterogeneity.

5.5. Method to control multiplicity

Since the analyses included in current SAP are subsequent analyses of IDEA data following the Grothey et al report, with key secondary outcome (OS) analyses, as well as the intention to allow extended exploratory subgroup analyses, the false discover rate method will be used to control type I error rate.

6. STATISTICAL REPORTING AND INTERPRETATION

6.1. Statistical reporting

Following the recent The New England Journal of Medicine New Guidelines for Statistical Reporting[3], point estimates of treatment duration effects, and standard error and/or two-sided 95% CIs will be reported for both pre-planned and ad hoc analyses. P-values will be reported **only** for treatment duration comparisons for which this SAP outlined the method for adjusting for multiplicity (i.e., controlling type I error rate). See section 7 for comparisons to be reported with p-values.

6.2. Results interpretation

Statistical significant claims of non-inferiority (i.e., 3 months of treatment is not worse than 6 months of treatment), superiority (i.e., 3 months of treatment is better than 6 months of treatment), or inferiority (i.e., 3 months of treatment is worse than 6 months of treatment) will be **only applicable** for the treatment duration comparisons which are associated with the pre-specified method to adjust for multiplicity, i.e. **multiple comparison adjusted p-values** are reported. The statistical significance thresholds are:

- One-sided, multiple comparison adjusted p-value < 0.025 for non-inferiority testing
- Two-sided, multiple comparison adjusted p-value < 0.05 for superiority testing

It is very important to recognize that non-significant p-value DOES NOT equate null hypothesis is true.

6.3. Guidance of conclusion(s) of this major subsequent analysis after Grothey et al report

The main conclusion regarding whether 3 months of treatment is non-inferior to 6 months of treatment will be made based on the following guidance:

- Including main statistical significance testing results reported in Grothey at al report, by including these in the multiple comparison adjustment
- Including statistical significance testing results reported on both primary endpoint of DFS and key secondary endpoint of OS, by including both in the multiple comparison adjustment
- Only based on the results of the comparisons which are pre-specified for multiple comparison adjusted p-value reporting

7. NON-INFERIORITY HYPOTHESIS TESTING REGARDING OS

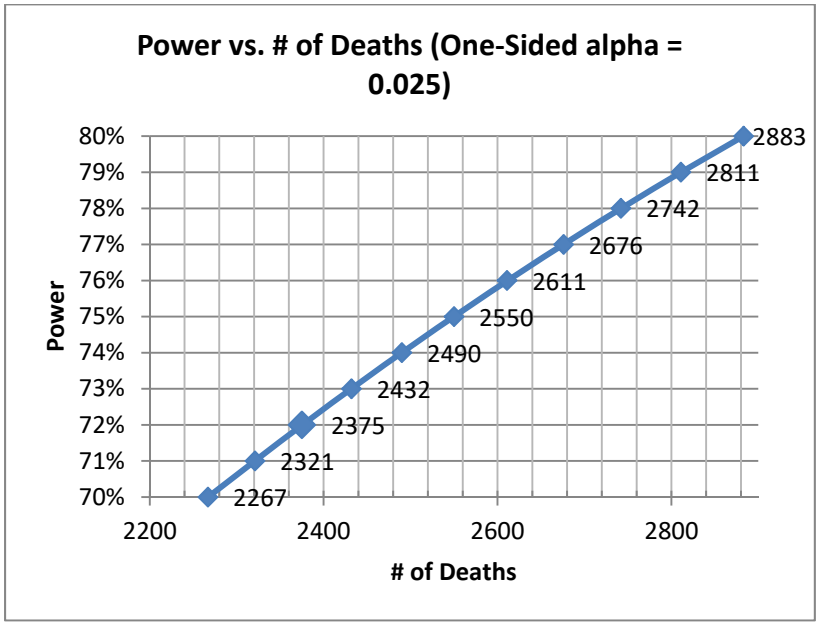
7.1. Determination of non-inferiority margin

When survival actualization after 10-year follow-up was performed, MOSAIC trial investigators reported 5-year OS rates of 76.0% (standard error [SE] 1.7%) and 71.7% (SE 1.8%) in patients receiving FOLFOX4 and LV5FU2, respectively. The estimated HR of comparing OS in FOLFOX4 arm to LV5FU2 arm was 0.80 (95% CI 0.66 to 0.96).[4] This corresponds to a 20% reduction of hazard of deaths by adding oxaliplatin to 5FU/LV.

In order to balance between benefits (relief from neurotoxicity) and cost (loss of OS efficacy) due to reducing 5FU/LV+oxaliplatin treatment duration by half, the maximum acceptable loss of treatment efficacy was set to 1/2 of the gain obtained by adding oxaliplatin to 5FU/LV established by MOSAIC trial. Hence the non-inferiority margin regarding OS endpoint was determined as 1/(0.8+(1-0.8)/2) = 1.11. Assuming exponential survival distribution and the 5-year OS rate in 6 months treatment arm of 76.0%, the HR of 1.11 translates to 5-year OS rate in 3 months treatment arm of 73.74%, i.e. 2.26% absolute reduction in 5-year OS rate. Hence, the non-inferiority hypothesis testing regarding OS consists with the following hypothesis:

- Null hypothesis: HR of comparing OS between 3 months vs. 6 months treatment ≥ 1.11
- Alternative hypothesis: HR of comparing OS between 3 months vs. 6 months treatment= 1.0

The following figure shows the relationship between power and observed number of death at the statistical significance level of one-sided alpha of 0.025, without controlling multiplicity.



Given the fact that all studies have completed accrual and approaching 5 years of median follow-up, we estimate 2400 to 2500 deaths will be observed at the time of analysis. The number of deaths will provide approximately 73% or higher power.

8. ANALYSIS PLAN

8.1. Patient characteristics

For patient characteristics per study and per treatment duration groups see Grothey et al.

8.2. Treatment compliance

For treatment compliance regarding therapy duration, completion of cycles, percent of dose delivered per agents, see Grothey et al.

8.3. Adverse events (AE)

AE profile pooling all six studies reported in Grothey et al may be updated if substantial new AE data were transferred by Dec 2019. These new AE data include, but not limited to, AE types which were not reported in Grothey et al, and late neurotoxicity which was aggregable across more than three studies.

8.4. Primary efficacy analysis

The purpose of this subsequent IDEA collaboration analysis is to provide updated or confirmed conclusion regarding whether 3 months of treatment is non-inferior to 6 months of treatment based on extended follow-up obtained on the patients enrolled on six IDEA trials. However, it is critical to control multiplicity. Therefore, we pre-specify efficacy analyses in this section.

8.4.1. Estimation

For DFS with updated data, the 3/4/5 year DFS rates and two-sided 95% CIS within each of the two duration arms, and the differences in 3/4/5 year DFS rates between two arms and two-sided 95% Cis, and stratified HR with two-sided 95% CI will be reported, 1) pooling all studies, 2) within regimen groups (FOLFOX vs. CAPOX), and 3) within T/N stage risk groups (T1-3 and N1 vs. T4 and/or N2).

For OS, the 5 year OS rates and two-sided 95% CIS within each of the two duration arms, and the differences in 5 year OS rates between two arms and two-sided 95% Cis, and stratified HR with two-sided 95% CI will be reported, 1) pooling all studies, 2) within regimen groups (FOLFOX vs. CAPOX), and 3) within T/N stage risk groups (T1-3 and N1 vs. T4 and/or N2).

8.4.2. Statistical significance testing

The non-inferiority margin for non-inferiority testing regarding OS is HR = 1.11. However, using upper bound of two-sided 95% CIs, in comparison to non-inferiority margin, is not appropriate for statistical significance testing any more, since these CIs are not adjusted for multiple comparisons across 1) what reported in Grothey et al report and current subsequent analyses; 2) DFS and OS analyses; 3) pooling all pts and within regimen and risk group subgroups. **Therefore, all statistical significance testing will be based on multiple comparison adjusted p-values.** The following comparisons will be pre-specified to be considered for multiple comparison adjustment:

1. DFS comparison pooling all patients, within FOLFOX and CAPOX subgroups, and within high and low risk subgroups. Total of 5 comparisons.
    a. The reported unadjusted p-values in Grothey et al will be used in false discovery rate adjustments
2. The updated DFS comparisons with updated DFS data pooling all patients, within FOLFOX and CAPOX subgroups, and within high and low risk subgroups. Total of 5 comparisons.
3. The OS comparisons pooling all patients, within FOLFOX and CAPOX subgroups, and within high and low risk subgroups. Total of 5 comparisons.

Thus, total of 10 comparisons (#2 and #3) in current analysis plan will report multiple comparison adjusted p-values for overall statistical inferences regarding whether 3 months of treatment is non-inferior to 6 months of treatment.

8.5. Pre-planned subgroup analyses

Additional subgroup analyses will be performed between duration groups within subgroups defined by T-stage (T1/2 vs. T3 vs. T4), N-stage (N1 vs. N2), number of lymph nodes examined (≥ 12 vs. < 12), tumor location (right vs. transverse vs. left colon), historical grade (high vs low), age (≤ 50 vs. 50-70 vs. ≥ 70), gender (male vs. female), baseline PS (0 vs. 1+) for both DFS and OS. These analyses are in exploratory nature and only report point estimates of HRs and two-sided 95% CIs. **NO formal statistical significance conclusions will be made for these subgroup analyses.**

9. REFERENCES

1. Grothey A, Sobrero AF, Shields AF, Yoshino T, Paul J, Taieb J, Souglakos J, Shi Q, Kerr R, Labianca R, Meyerhardt JA, Vernerey D, Yamanaka T, Boukovinas I, Meyers JP, Renfro LA, Niedzwiecki D, Watanabe T, Torri V, Saunders M, Sargent DJ, Andre T, Iveson T. Duration of Adjuvant Chemotherapy for Stage III Colon Cancer. N Engl J Med. 2018 Mar 29; 378 (13):1177-1188PMID: 29590544 PMCID: 6426127 DOI: 10.1056/NEJMoa1713709

2. Andre T, Iveson T, Labianca R, Meyerhardt JA, Souglakos I, Yoshino T, Paul J, Sobrero A, Taieb J, Shields AF, Ohtsu A, Grothey A, Sargent DJ, for the IDEA Steering Committee. The IDEA (International Duration Evaluation of Ajuvant Chemotherapy) Collaboration: Prospective Combined Analysis of Phase III Trials Investigating Duration of Adjuvant Therapy with the FOLFOX (FOLFOX4 or Modified FOLFOX6) or CAPOX (3 versus 6 months) Regimen for Patients with Stage III Colon Cancer: Trial Design and Current Status. Curr Colorectal Cancer Rep (2013) 9:261-269

3. Harrington D, D'Agostino RB, Gatsonis C, Hogan JW, Hunter DJ, Normand S-LT, Drazen JM, Hamel MB. New guidelines for statistical reporting in the Journal. The New England Journal of Medicine, 2019; 318;3:285

4. Andre T, de Gramont A, Vernerey D, et al. Adjuvant Fluorouracil, Leucovorin, and Oxaliplatin in Stage II to III Colon Cancer: Updated 10-Year Survival and Outcomes According to BRAF Mutation and Mismatch Repair Status of the MOSAIC Study. J Clin Oncol 2015;33:4176-87.