TO: Raymond P. Bain, PhD

FROM: Joshua Chen, PhD

SUBJECT: MK-0966 Combined Mortality Analysis
Protocol 091 + Protocol 078

DATE: April 8, 2001

Summary:

In this report, results from the combined mortality analysis for MK-0966 Protocols 091 and 078 are provided. The cut-off date for the on-going prevention trial Protocol 078 was 03/23/2001. Two methods were used to analyze the data:

1. Combined Intention-to-Treat (ITT) Analysis
2. Combined On-Drug Analysis

For the ITT Analysis, any death which occurred within 14 days after discontinuation of *study* was counted as an event. The combined data for the ITT analysis had two components: data used for ITT analysis in the prevention trial Protocol 078 and data used for the 0-12 Month ITT Analysis in the first AD treatment study Protocol 091.

For the On-Drug Analysis, any death which occurred on drug or within 14 days after discontinuation of *study drug* was counted as an event. Data from the On-Drug Analysis in Protocol 078 and from the 0-12 Month On-Drug Analysis in Protocol 091 were combined.

For each of the two combined analyses, the following results are provided:

*.1. Summary of Main Results from Individual Analysis

*.2. Combined Data from Protocols 078 and 091

*.3. Time to All-Cause Mortality Analysis

*.4. Subgroup Analysis by Age and Gender

1. Combined ITT Analysis

1.1. Summary of Main Results From Individual ITT Analysis

1.1.1 Baseline Characteristics

Table 1.1a Treatment Study Protocol 091

	MK-0966 (N=346)	Placebo (N=346)
Age		
Mean (std)	75.6 (8.3)	75.0 (8.8)
Median	77.0	76.0
Female	54.1%	52.3%

Table 1.1b Prevention Study Protocol 078

	MK-0966 (N=723)	Placebo (N=732)
Age		
Mean (std)	75.1 (6.0)	74.8 (6.0)
Median	75.0	75.0
Female	34.2%	31.2%

1.1.2 Patient Status

Table 1.2a 0-12 Month ITT Analysis For Protocol 091

	MK-0966 (N=346)	Placebo (N=346)
Number of Deaths (%)	13 (3.8)	3 (0.9)
Number of Discon* (%)	77 (22.3)	70 (20.2)
Number still in Study (%)	256 (74.0)	273 (78.9)
* Discontinuation of study before 12-month AND alive 14 days after discontinuation		

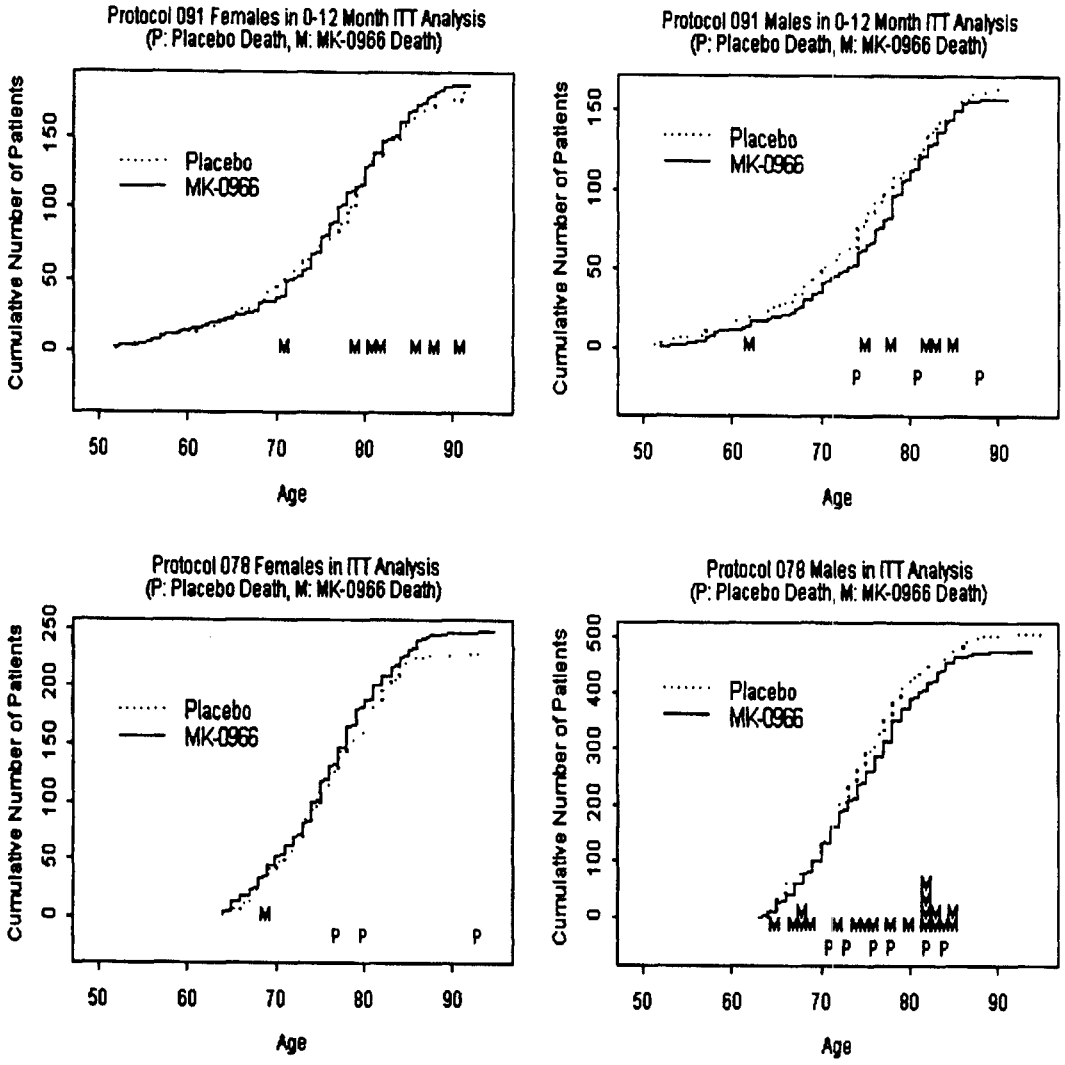
Table 1.2b ITT Analysis For Protocol 078

	MK-0966 (N=723)	Placebo (N=732)
Number of Deaths (%)	21 (2.9)	9 (1.2)
Number of Discon* (%)	290 (40.1)	259 (35.4)
Number still in Study (%)	412 (57.0)	464 (63.4)
* Discontinuation of study AND alive 14 days after discontinuation		

The mortality frequency was 16/692=2.3% in the treatment study Protocol 091 and 30/1455=2.1% in the prevention trial Protocol 078. The median follow up was 1.00 year in Protocol 091 and 1.70 years in Protocol 078.

Figure 1.1 summarizes the mortality events from Protocol 091 and 078. The top two panels correspond to females and males respectively in Protocol 091 and the bottom two panels correspond to Protocol 078. The X-axis is patient age and Y-axis is the cumulative number of patients. Each death is marked at the corresponding age: an M refers to a death in the MK-0966 arm and a P refers to a death in the placebo arm. Figure 1.1 shows the distribution of mortality event across protocol, gender and age. Also, since age was a significant predictor of death (section 1.1.4), this graph can help to detect an unequal number of older patients who were at higher risk between the placebo and the MK-0966 arms.

Figure 1.1 Summary of the Mortality Events for ITT Analysis



1.1.3 Survival Analysis

Figure 1.2 Kaplan-Meier Survival Estimates for MK-0966 and Placebo by Individual Protocol

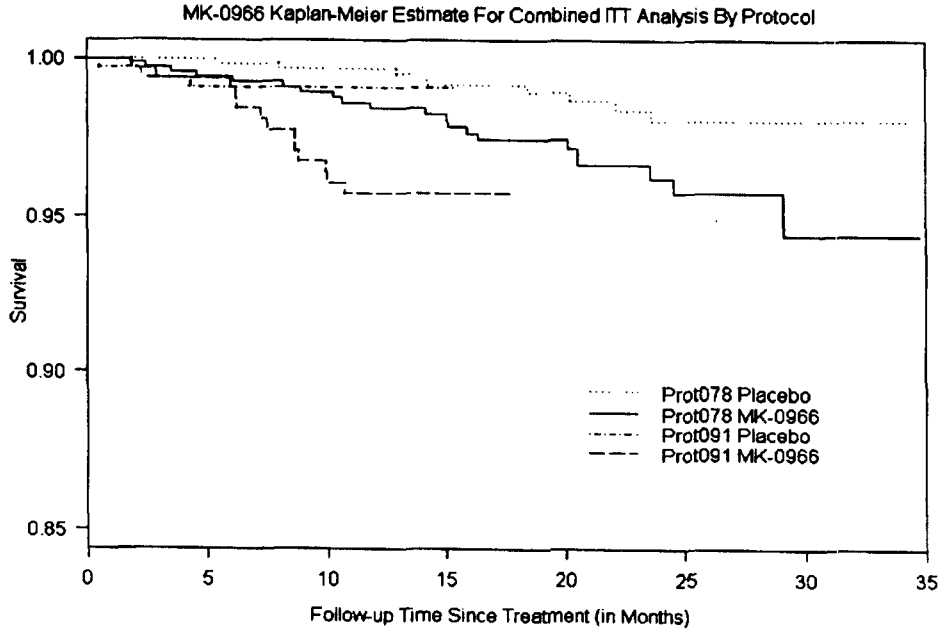
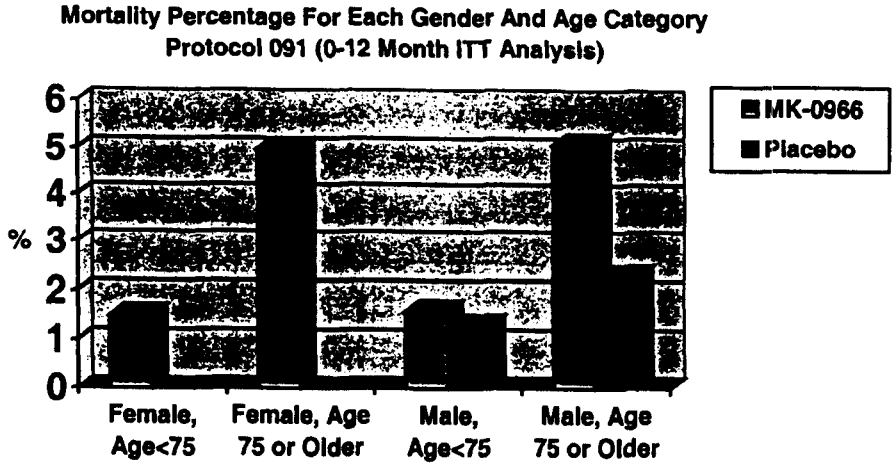


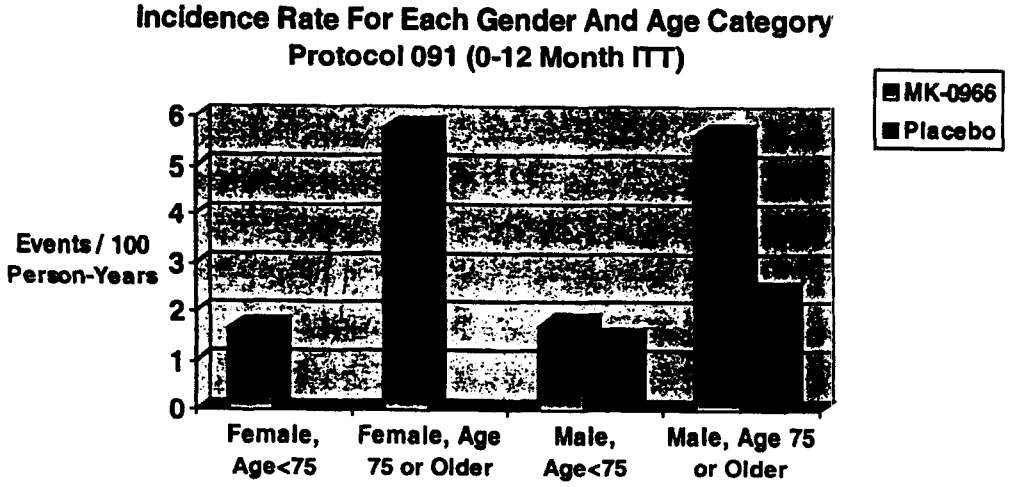
Figure 1.2 shows that patients in Protocol 091 had higher risk of death than those in Protocol 078. The logrank comparison between MK-0966 and Placebo indicated that survival was worse for patients receiving MK-0966 in Protocol 091 (p=0.010) and in Protocol 078 (p=0.015).

1.1.4 Subgroup Analysis by Age and Gender

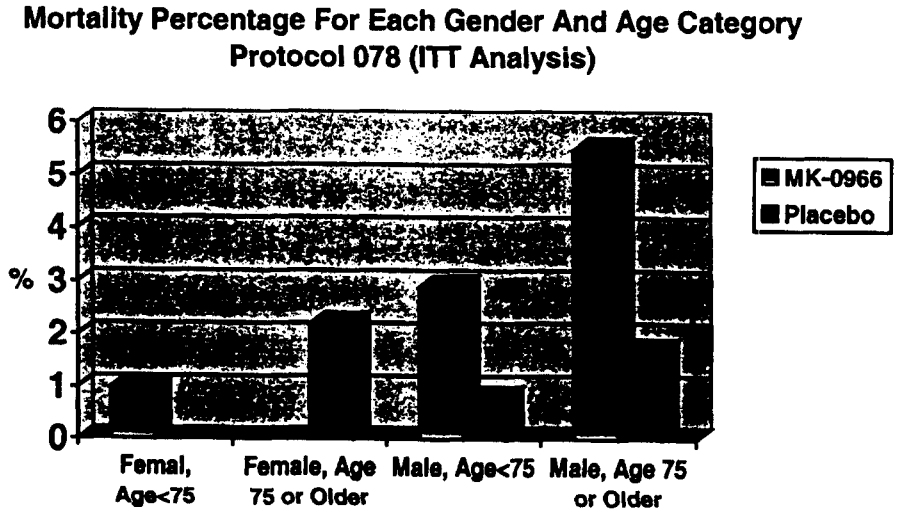
The following charts summarize the mortality frequency (percentage of death) and incidence rate (ratio with the number of events as the numerator and the total person-years at risk as



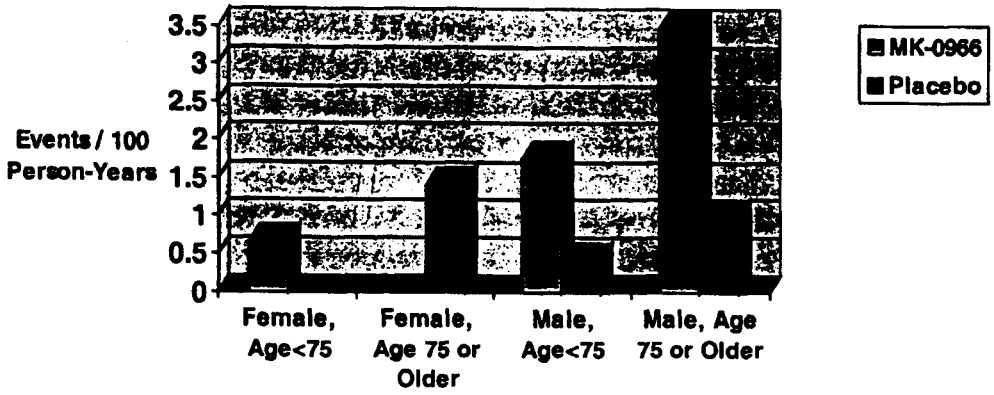
the denominator) for each age and gender category.



From the mortality frequency and incidence rate charts for Protocol 091, patients receiving MK-0966 had a greater chance to die across all of the four age and gender categories. In the MK-0966 arm, *Age* seemed to be a predictor of death while *Gender* was not. For placebo group, there was a difference between females and males. Using a Cox Proportional Hazards model, we found that *Age* and *Treatment* were statistically significant (p=0.016 for *Age* and 0.021 for *Treatment*). After adjusting for *Age*, the hazard ratio between MK-0966 and placebo was **4.43** (95% CI: 1.26 to 15.53).



Incidence Rate For Each Gender And Age Category
Protocol 078 (ITT Analysis)



From the mortality frequency and incidence rate charts for Protocol 078, males aged 75 or older had the highest risk of death. Both *Age* and *Gender* seemed to be predictors of death. Using a Cox Proportional Hazards model, we found that there might be an interaction effect between *Gender* and *Treatment* (p=0.061). *Age, Gender* and *Treatment* were all statistically significant (p=0.005 for *Age*, 0.023 for *Gender* and 0.019 for *Treatment*). After adjusting for *Age* and *Gender*, the hazard ratio between MK-0966 and placebo was **2.55** (95% CI: 1.17 to 5.56).

1.2. Combined Data Set For ITT Analysis

The combined data set for ITT Analysis included 2147 subjects (692 from Protocol 091 and 1455 from Protocol 078). There were 1069 subjects in the MK-0966 arm (346 from Protocol 091 and 723 from Protocol 078) and 1078 subjects in the placebo arm (346 from Protocol 091 and 732 from Protocol 078).

1.2.1 Baseline Characteristics

Table 1.2.1. Baseline Characteristics (Combined ITT Analysis)

	MK-0966 (N=1069)	Placebo (N=1078)
Age (years)		
Mean (std)	75.3 (6.8)	74.9 (7.0)
Median	76.0	75.0
Female	40.6%	37.9%
From Protocol 091 (AD)	32.4%	32.1%

1.2.2 Mortality Frequency

Table 1.2.2 summarize the mortality frequency for the combined ITT data.

Table 1.2.2 Mortality Frequency (Combined ITT Analysis)

Number of Deaths (%)	MK-0966 (N=1069)	Placebo (N=1078)
Total *	34 (3.2)	12 (1.1)
Protocol 091 (AD) **	13 (38.2%)	3 (25%)
Protocol 078 **	21 (61.8%)	9 (75%)

* total number of deaths in each treatment arm (% number of patients in the treatment arm)
** number of deaths from individual protocol (% total deaths in the treatment arm)

1.2.3 Can We Combine Protocols 091 and 078?

Protocols 091 and 078 were different studies with different patient populations. From Figure 1.2, patients in Protocol 091 had higher risk of death than those in Protocol 078. It may not be appropriate to combine the two protocols if there is a strong interaction between *Protocol* and *Treatment*.

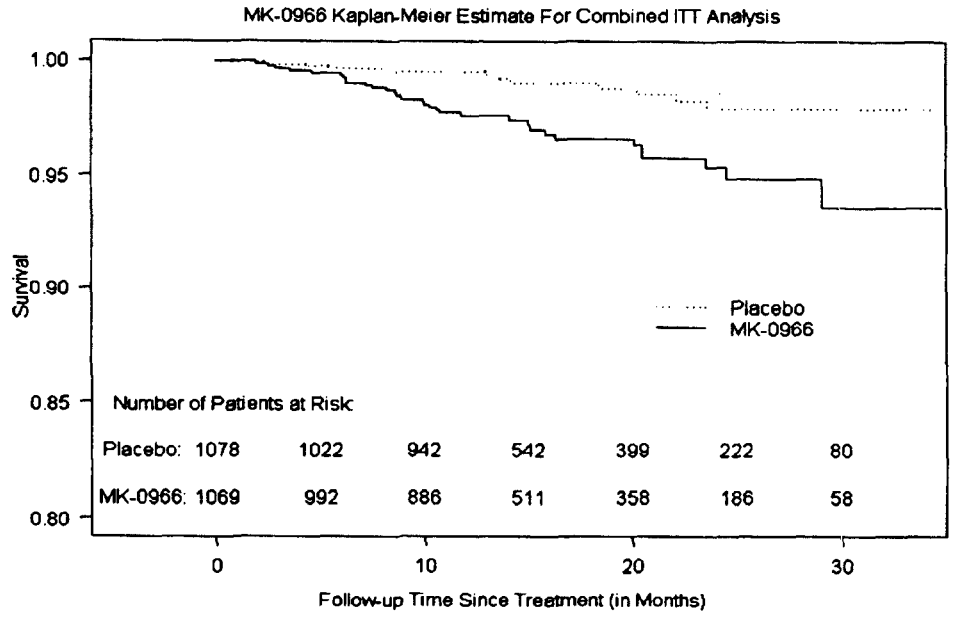
Cox Proportional Hazards model was applied to test if the impact of *Age, Gender* and *Treatment* on the mortality hazard was different between the two protocols. The p-values for the combinations between *Protocol* and *Age, Gender* and *Treatment* were 0.79, 0.29 and 0.47 respectively. This indicated that the effect of *Age, Gender* and *Treatment* on the mortality hazard might not be different between the two protocols.

1.3 All-Cause Mortality Analysis

1.3.1 Kaplan-Meier Estimate of Survival

The Kaplan-Meier estimates of the survival curves for the ITT Analysis is given in Figure 1.3.

Figure 1.3. KM Estimate for the Combined ITT Analysis



The Kaplan-Meier curves are the estimated survival for the mixed patient population. Since the duration of 0-12 Month ITT Analysis for Protocol 091 was 12 months, patients at risk after 12 months were essentially those from Protocol 078. Therefore, only the early parts of the survival curves were estimated from the combined data for both protocols. The late parts were actually based on the data from Protocol 078.

For Combined ITT Analysis, the logrank test comparing MK-0966 and placebo indicated that survival was worse for patients receiving MK-0966 ($p<0.001$).

Evaluation of Statistical Models:

The three-term combination *Age*Gender*Treatment* was not statistically significant in a Cox Proportional Hazards model (p=0.83). No statistically significant combinations between *Age*, *Gender* and *Treatment* were found in the combined ITT analysis (all p-values > 0.30).

If all combinations were removed from the model, *Age, Gender, Treatment* and *Protocol* were all significant (p<0.001 for *Age*, 0.017 for *Gender*, 0.001 for *Treatment* and 0.006 for *Protocol*). The hazard ratio between MK-0966 and placebo was **2.99** (95% CI: 1.55 to 5.77) from this model. Other interpretation from the model:

- If subject A was one year older than subject B, A was more likely to die and the mortality hazard ratio between A and B was 1.09 (95% CI: 1.04 to 1.14).

- Females were less likely to die than males. The mortality hazard ratio was 0.43 (95% CI: 0.22 to 0.86).

- Patients in Protocol 091 had a greater chance to die than subjects in Protocol 078. The hazard ratio was 2.89 (95% CI: 1.36 to 6.13).

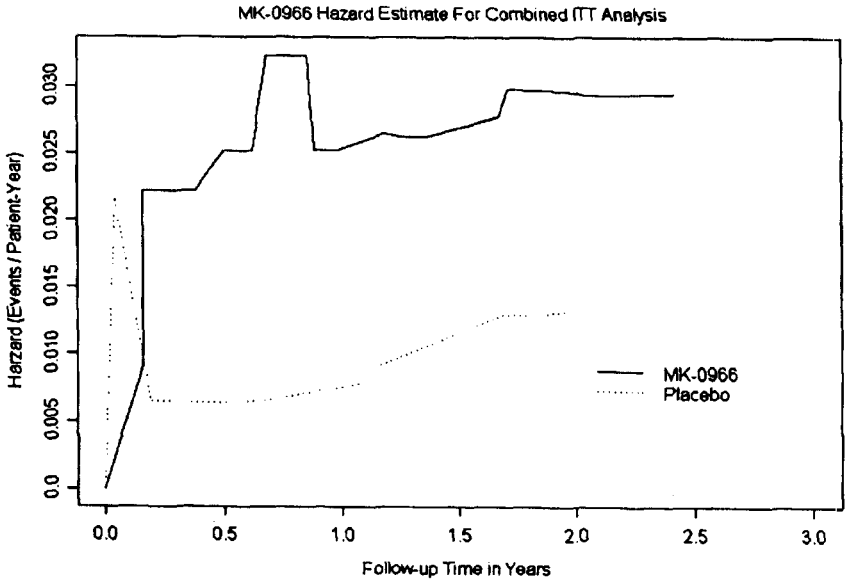
Another Cox Proportional Hazards model which did not adjust for any of the significant predictors *Age*, *Gender* and *Protocol* gave a similar hazard ratio estimate between MK-0966 and placebo: **3.04** with 95% CI (1.57, 5.86).

1.3.2. Mortality Hazard Rate

The incidence rate, which is defined as a ratio with the number of events as the numerator and the total person-years at risk as the denominator, was 0.0078 events per person-year (12/1548) for placebo and 0.0234 events per person-year (34/1452) for MK-0966. The interpretation of the incidence rates should be based upon the mixed patient population.

The hazard rate derived from the combined ITT Analysis is plotted in Figure 1.4. The unit for the Y-axis is events per person-year follow up such that the result could be comparable to the average hazard - incidence rate.

Figure 1.4. Hazard Estimate (Combined ITT Analysis)



1.4 Mortality Analysis by Subgroups

In this section, the combined ITT mortality is analyzed by the following patient subgroups.

Age groups: Age < 75 years
Age greater than or equal to 75 years

Gender: Female
Male

This subgroup mortality analysis section consists of three parts:

- Mortality frequency by subgroup
- Time to all-cause mortality by subgroup
- Incidence rates

1.4.1 Mortality Frequency by Subgroup

Table 1.4.1 presents the number of deaths by age category, gender and the combination of age category and gender. The mortality rate was higher in the patients aged 75 year or older for both males and females.

Table 1.4.1 Mortality Frequency by Subgroup (Combined ITT Analysis)

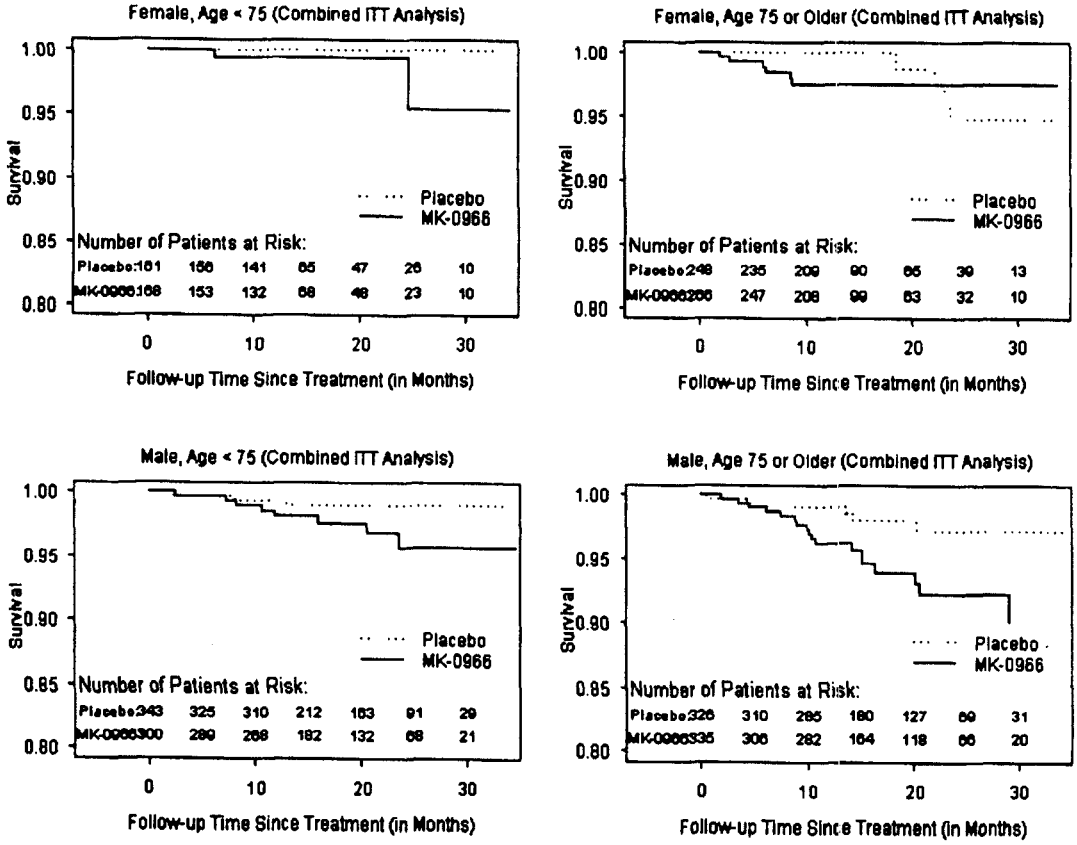
n/N (%)	MK-0966	Placebo	p-value
Age < 75 Years	10/468 (2.1)	3/504 (0.6)	0.049 *
Age 75 Years or Older	24/601 (4.0)	9/574 (1.6)	0.013 *
Female	8/434 (1.8)	3/409 (0.7)	0.226
Male	26/635 (4.1)	9/669 (1.4)	0.003 *
Female, Age < 75 Years	2/168 (1.2)	0/161 (0.0)	0.499
Female, Age 75 Years or Older	6/266 (2.3)	3/248 (1.2)	0.506
Male, Age < 75 Years	8/300 (2.7)	3/343 (0.9)	0.125
Male, Age 75 Years or Older	18/335 (5.4)	6/326 (1.8)	0.021 *

N = Number of randomized patients in the subgroup
n = Number of deaths in the subgroup
Fisher's two-tail exact test was used to compare the mortality rates.
* : statistically significant at level 0.05

1.4.2. Time to All-Cause Mortality by Subgroup

Figure 1.5 presents the Kaplan-Meier estimates of the survival curves by combination of age category and gender. The four panels correspond to females younger than 75, females aged 75 or older, males younger than 75 and males aged 75 or older.

Figure 1.5. Kaplan-Meier Estimates for Age and Gender Subgroups (Combined ITT Analysis)

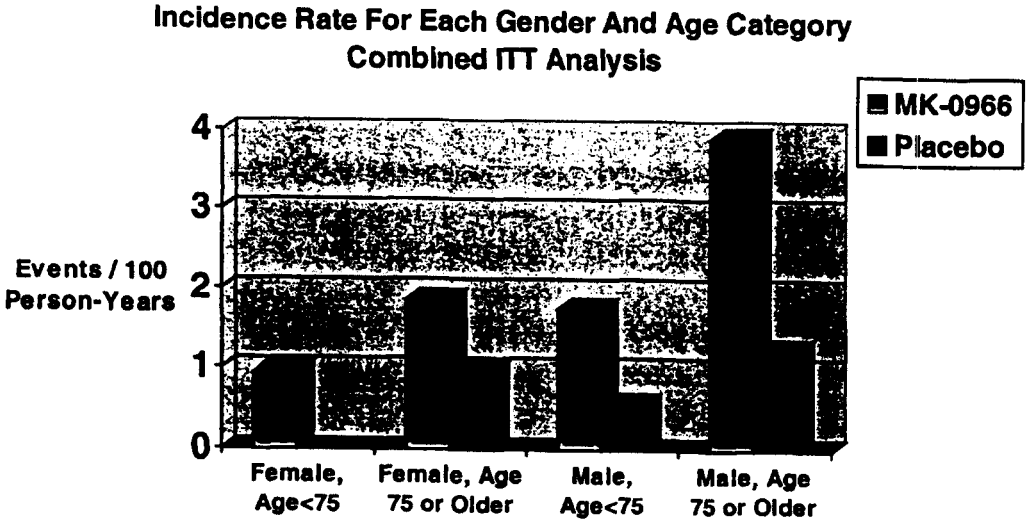


1.4.3 Mortality Incidence Rate

The incidence rate is defined as a ratio with the number of events as the numerator and the total person-years at risk as the denominator. It is the average hazard of death over the follow up period. The incidence for each combination subgroup is given in Table 1.4.2 and visually demonstrated in a chart. Note here the incidence is for the mixed patient population.

Table 1.4.2 Incidence Rate By Subgroup (Combined ITT Analysis)

Incidence rate (number of events / person-years follow up)	MK-0966	Placebo
Female, Age < 75	0.0095 (2/211)	0.0000 (0/213)
Female, Age 75 Years or Older	0.0186 (6/323)	0.0095 (3/317)
Male , Age < 75	0.0175 (8/457)	0.0056 (3/536)
Male , Age 75 Years or Older	0.0390 (18/461)	0.0125 (6/481)
Incidence rate in events per person-year follow up		



2. Combined On-Drug Analysis

2.1. Summary of Main Results From Individual On-Drug Analysis

2.1.1 Baseline Characteristics

Table 2.1a Treatment Study Protocol 091

	MK-0966 (N=346)	Placebo (N=346)
Age		
Mean (std)	75.6 (8.3)	75.0 (8.8)
Median	77.0	76.0
Female	54.1%	52.3%

Table 2.1b Prevention Study Protocol 078

	MK-0966 (N=721)	Placebo (N=729)
Age		
Mean (std)	75.1 (6.0)	74.8 (6.0)
Median	75.0	75.0
Female	34.1%	30.9%
Five patients were randomized but never received study drug: 3/5 from placebo and 2/5 from MK-0966		

2.1.2 Mortality Frequency

Table 2.2 Mortality for On-Drug Analysis by Protocol

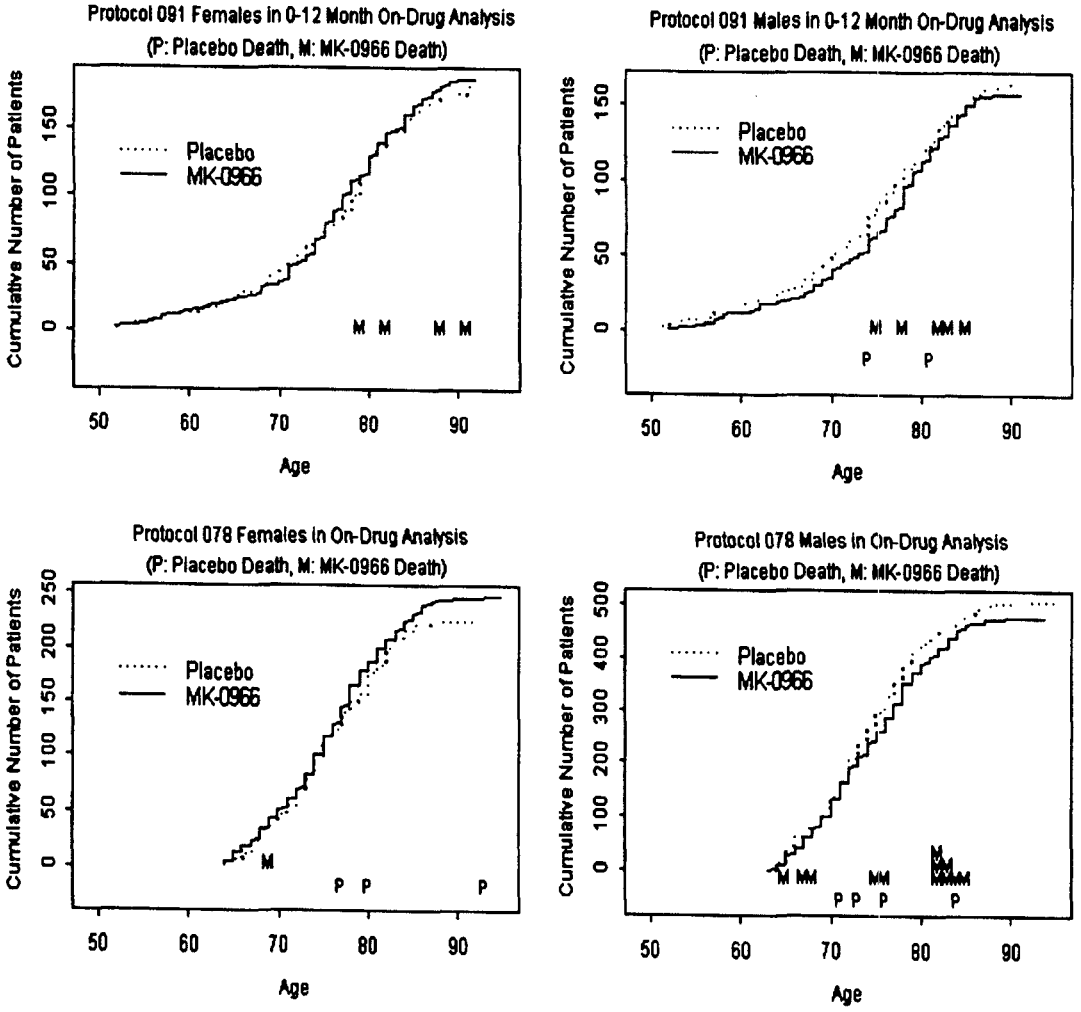
n/N (%)	MK-0966	Placebo
Protocol 091 0-12 Month	9 / 346 (2.6)	2 / 346 (0.6)
Protocol 078	13 / 721 (1.8)	7 / 729 (1.0)
N = Number of patients n = Number of deaths Include deaths which occurred within 14 days after discontinuation of study drug		

The mortality frequency was 11/692=1.6% in the treatment study Protocol 091 and 20/1450=1.4% in the prevention trial Protocol 078. The median follow up was 1.00 year in Protocol 091 and 1.52 years in Protocol 078.

Figure 2.1 summarizes the mortality events for On-Drug Analysis from Protocol 091 and 078. The top two panels correspond to females and males respectively in Protocol 091 and the bottom two panels correspond to Protocol 078. The X-axis is patient age and Y-axis is the cumulative number of patients. Each death is marked at the corresponding age: an M

refers to a death in the MK-0966 arm and a P refers to a death in the placebo arm. Figure 2.1 shows the distribution of mortality event across protocol, gender and age. Also, since age was a significant predictor of death (section 2.1.4), this graph can help to detect unequal number of older patients who were at higher risk between the placebo and the MK-0966 arms.

Figure 2.1 Summary of the Mortality Event for On-Drug Analysis



2.1.3 Survival Analysis

Figure 2.2 Kaplan-Meier Survival Estimates For MK-0966 and Placebo by Individual Protocol (Combined On-Drug Analysis)

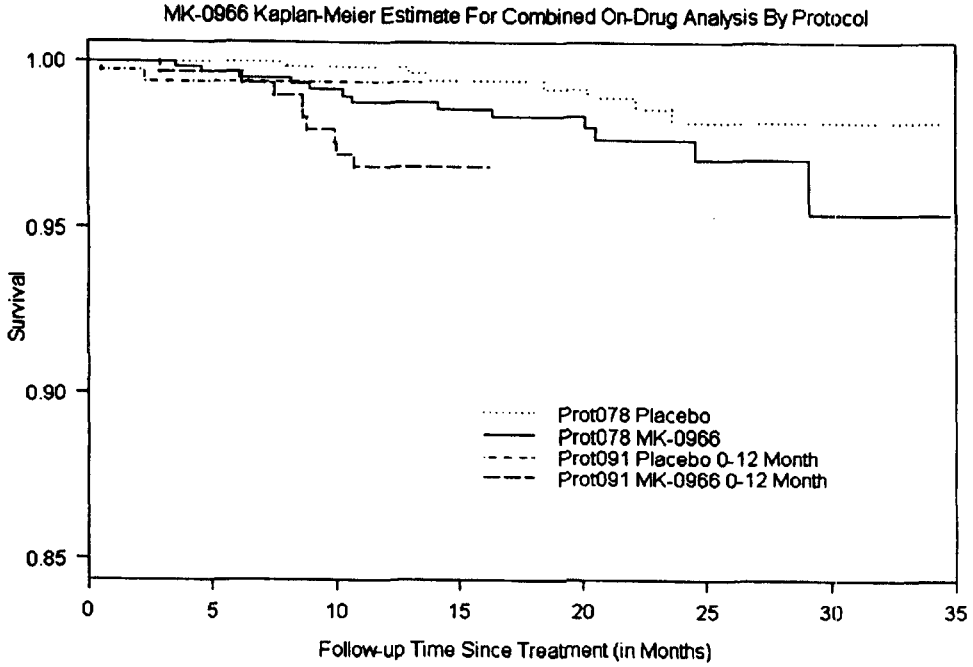


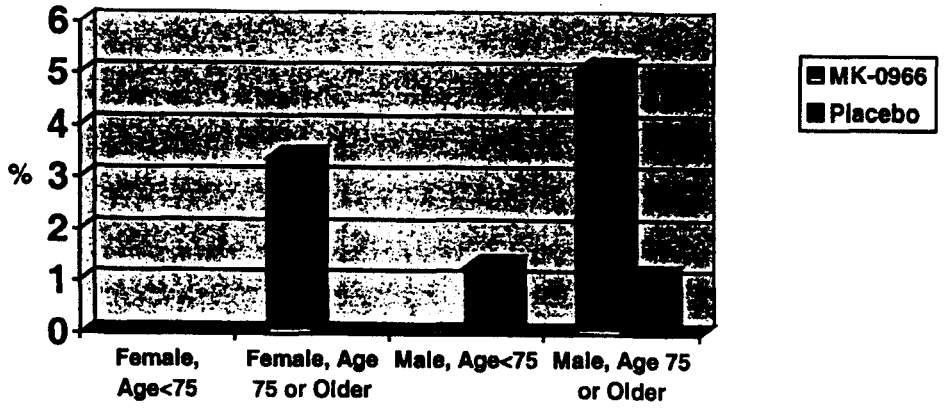
Figure 2.2 shows that patients in Protocol 091 had higher risk of death than those in Protocol 078. The logrank comparison between MK-0966 and Placebo indicated that survival was worse for patients receiving MK-0966 in Protocol 091 (p=0.028). However, interpretation of the survival difference should take the following facts into account: the number of mortality events was small (9 in MK-0966 and 2 in placebo); the survival curves crossed indicating that the mortality events in the placebo arm occurred sooner than those in the MK-0966 arm. There was no statistically significant difference between MK-0966 and placebo in Protocol 078 (p=0.10).

2.1.4 Subgroup Analysis by Age and Gender

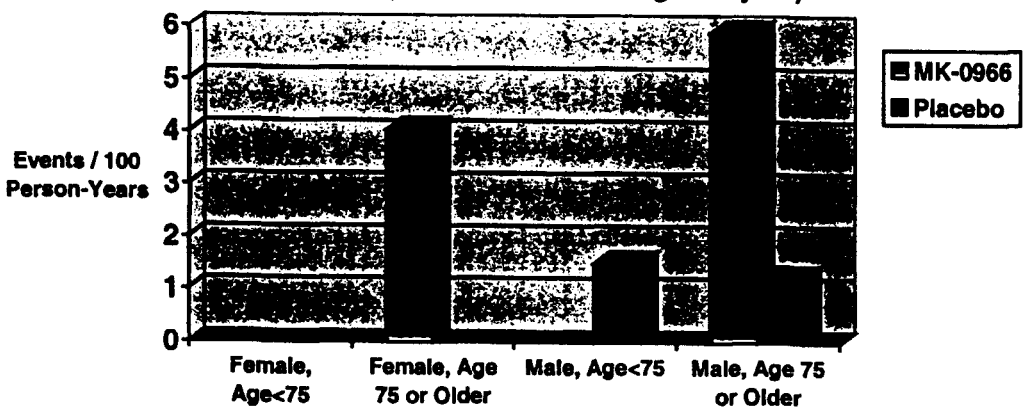
The following charts summarize the mortality frequency (percentage of death) and incidence rate (ratio with the number of events as the numerator and the total person-years at risk as the denominator) for each age and gender category. The mortality frequency chart presents the crude mortality data while the incidence rate chart adjusts for the duration of patient at risk.

From the On-Drug analysis of the mortality frequency and incidence rate charts for Protocol 091, patients older than 75 who were receiving MK-0966 had a greater chance of death than younger patients. The highest MK-0966 mortality rate was recorded in males aged 75 or older. Using a Cox Proportional Hazards model, we found that *Age* and *Treatment* were statistically significant (p=0.010 for *Age* and 0.049 for *Treatment*). *Gender* was not significant (p=0.20). After adjusting for *Age*, the hazard ratio between MK-0966 and placebo was **4.68** (95% CI: 1.01 to 21.68).

Mortality Percentage For Each Gender And Age Category
Protocol 091 (0-12 Month On-Drug Analysis)

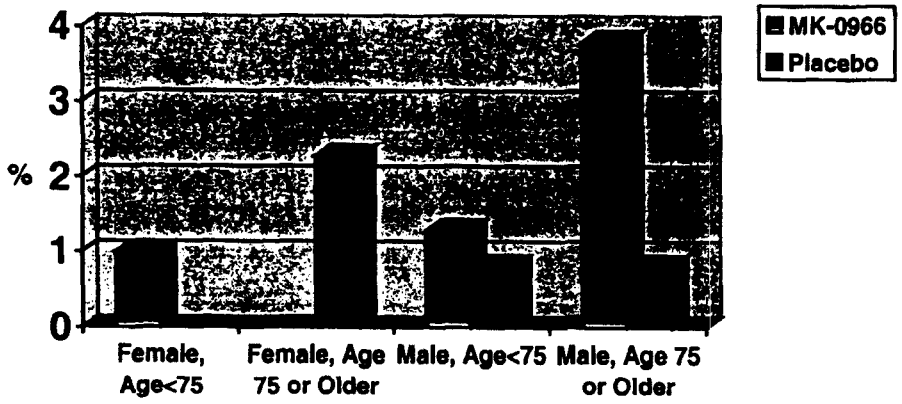


Incidence Rate For Each Gender And Age Category
Protocol 091 (0-12 Month On-Drug Analysis)

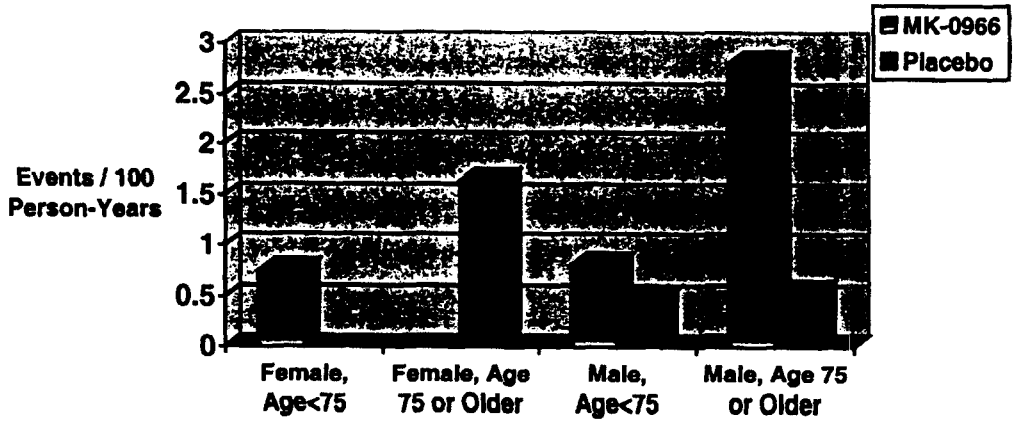


From the On-Drug analysis of the mortality frequency and incidence rate charts for Protocol 078, the highest MK-0966 mortality rate was recorded in males aged 75 or older. The incidence rate was higher in the MK-0966 arm for all combinations of age category and gender except for females aged 75 or older. Using a Cox Proportional Hazards model, we found that there might be an interaction between *Gender* and *Treatment* (p=0.076). *Age* was a statistically significant predictor of death (p=0.008). *Gender* and *Treatment* were not statistically significant (p=0.20 *Gender* and 0.11 for *Treatment*). After adjusting for *Age*, the hazard ratio between MK-0966 and placebo was **2.07** (95% CI: 0.82 to 5.19).

Mortality Percentage For Each Gender And Age Category
Protocol 078 (On-Drug Analysis)



Incidence Rate For Each Gender And Age Category
Protocol 078 (On-Drug Analysis)



2.2. Combined Data Set For On-Drug Analysis

The combined data set for On-Drug analysis included 2142 subjects (692 were from Protocol 091 and 1450 from Protocol 078). There were 1067 subjects in the MK-0966 arm (346 from Protocol 091 and 721 from Protocol 078) and 1075 subjects in the placebo arm (346 from Protocol 091 and 729 from Protocol 078).

2.2.1 Baseline Characteristics

Table 2.2.1. Baseline Characteristics (Combined On-Drug Analysis)

	MK-0966 (N=1067)	Placebo (N=1075)
Age (years)		
Mean (std)	75.3 (6.8)	74.9 (7.0)
Median	76.0	75.0
Female	40.6%	37.8%
From Prot091 (AD)	32.4%	32.2%

2.2.2 Mortality Frequency

Table 2.2.2 Mortality Frequency (Combined On-Drug Analysis)

Number of Deaths (%)	MK-0966 (N=1067)	Placebo (N=1075)
Total *	22 (2.1)	9 (0.8)
Protocol 091 (AD) **	9 (40.9%)	2 (22.2%)
Protocol 078 **	13 (59.1%)	7 (77.8%)

* total number of deaths in each treatment arm (% number of patients in the treatment arm)
** number of deaths from individual protocol (% total deaths in the treatment arm)

2.2.3 Can We Combine Protocols 091 and 078?

Protocols 091 and 078 were different studies with different patient populations. From Figure 2.2, patients in Protocol 091 had higher risk of death than those in Protocol 078. It may not be appropriate to combine the two protocols if there is a strong interaction between *Protocol* and *Treatment*.

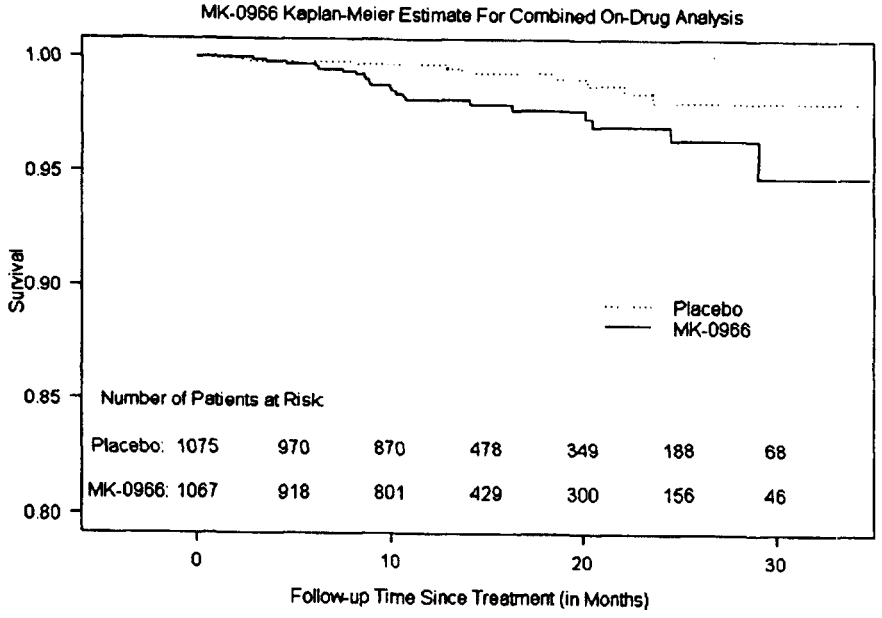
Cox Proportional Hazards model was applied to test if the impact of *Age, Gender* and *Treatment* on the mortality hazard was different between the two protocols. The p-values for the combinations between *Protocol* and *Age, Gender* and *Treatment* were 0.50, 0.93 and 0.38 respectively. This indicated that the effect of *Age, Gender* and *Treatment* on the mortality hazard might be the same for the two protocols.

2.3 All-Cause Mortality Analysis

2.3.1 Kaplan-Meier Estimate of Survival

The Kaplan-Meier estimates of the survival curves for the Combined On-Drug Analysis is given in Figure 2.3.

Figure 2.3. KM Estimate for the Combined On-Drug Analysis



The Kaplan-Meier curves are the estimated survival for the mixed patient population. Since the maximum duration of 0-12 Month On-Drug Analysis for Protocol 091 was 12 months, patients at risk after 12 months were essentially those from Protocol 078. Therefore, only the early parts of the survival curves were estimated from the combined data for both protocols. The late parts were actually based on the data from Protocol 078.

For Combined On-Drug Analysis, the logrank test comparing MK-0966 and placebo indicated that survival was worse for patients receiving MK-0966 (p=0.008).

Evaluation of Statistical Models:

The three-term combination *Age*Gender*Treatment* was not statistically significant in a Cox Proportional Hazards model (p=0.47). None of the combinations between *Age*, *Gender* and *Treatment* was found to be statistically significant in the combined On-Drug analysis (all p-values > 0.30).

If all combinations were removed from the model, *Gender* was marginally non-significant (p=0.067). *Age*, *Treatment* and *Protocol* were all significant (p<0.001 for *Age*, 0.013 for *Treatment* and 0.037 for *Protocol*). The hazard ratio between MK-0966 and placebo was **2.68** (95% CI: 1.23 to 5.82) from this model. Other interpretation from the model:

- If subject A was one year older than subject B, A was more likely to die and the mortality hazard ratio between A and B was 1.12 (95% CI: 1.05 to 1.18).

- Females might be less likely to die than males. The mortality hazard ratio was 0.46 (95% CI: 0.20 to 1.05).

- Patients in Protocol 091 had a greater chance to die than subjects in Protocol 078. The hazard ratio was 2.67 (95% CI: 1.06 to 6.70).

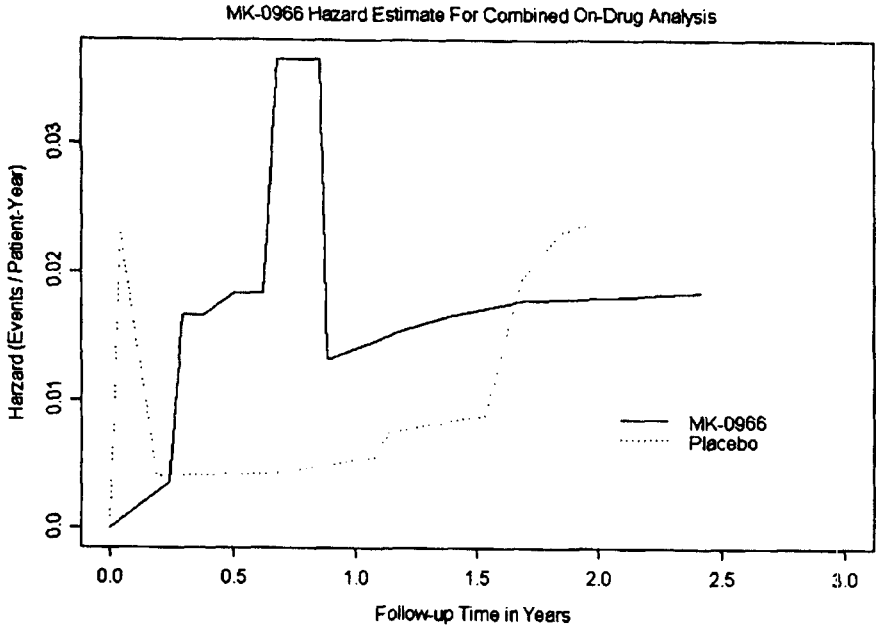
Another Cox Proportional Hazards model which did not adjust for any of the predictors *Age*, *Gender* and *Protocol* gave a similar hazard ratio estimate between MK-0966 and placebo: **2.72** with 95% CI (1.25, 5.91).

2.3.2. Mortality Hazard Rate

The incidence rate, which is defined as a ratio with the number of events as the numerator and the total person-years at risk as the denominator, was 0.0063 events per person-year (9/1427) for placebo and 0.0168 events per person-year (22/1307) for MK-0966. The interpretation of the incidence rates should be based upon the mixed patient population.

The hazard rate derived from the combined On-Drug Analysis is plotted in Figure 2.4. The unit for the Y-axis is events per person-year follow up such that the result could be comparable to the average hazard - incidence rate.

Figure 2.4. Hazard Estimate For Combined On-Drug Analysis



2.4 Mortality Analysis by Subgroups

In this section, the combined On-Drug mortality is analyzed by the following patient subgroups.

Age groups: Age < 75 years
Age greater than or equal to 75 years

Gender: Female / Male

This subgroup mortality analysis section consists of three parts:

- Mortality frequency by subgroup
- Time to all-cause mortality by subgroup
- Incidence rates

2.4.1 Mortality Frequency by Subgroup

Table 2.4.1 presents the number of deaths by age category, gender and the combination of age category and gender. The mortality rate was higher in the patients aged 75 year or older for both males and females.

Table 2.4.1 Mortality Frequency by Subgroup (Combined On-Drug Analysis)

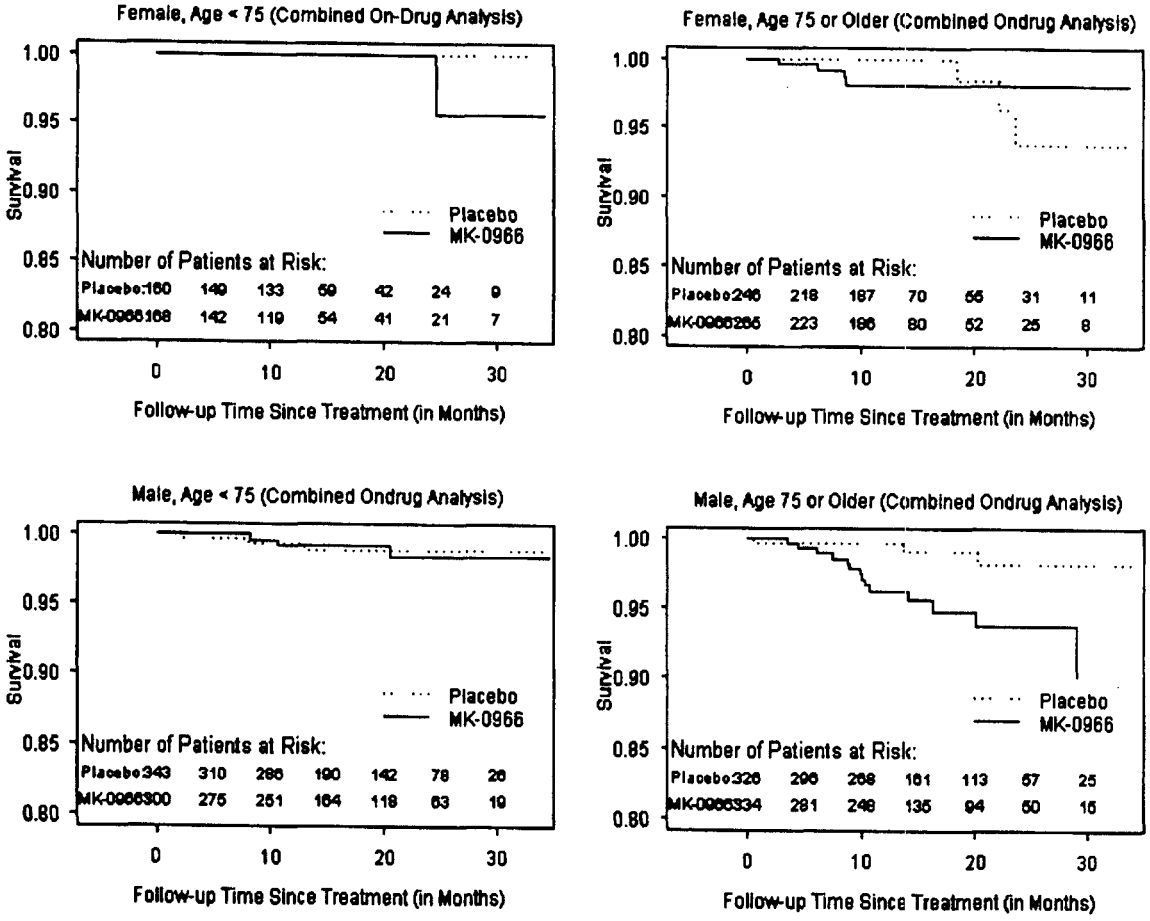
n/N (%)	MK-0966	Placebo	p-value
Age < 75 Years	4/468 (0.9)	3/503 (0.6)	0.717
Age 75 Years or Older	18/599 (3.0)	6/572 (1.1)	0.022 *
Female	5/433 (1.2)	3/406 (0.7)	0.726
Male	17/634 (2.7)	6/669 (0.9)	0.019 *
Female, Age < 75 Years	1/168 (0.6)	0/160 (0.0)	1.000
Female, Age 75 Years or Older	4/265 (1.5)	3/246 (1.2)	1.000
Male, Age < 75 Years	3/300 (1.0)	3/343 (0.9)	1.000
Male, Age 75 Years or Older	14/334 (4.2)	3/326 (0.9)	0.012 *

N = Number of randomized patients in the subgroup
n = Number of deaths in the subgroup
Fisher's two-tail exact test was used to compare the mortality rates.
* : statistically significant at level 0.05

2.4.2. Time to All-Cause Mortality by Subgroup

Figure 2.5 presents the Kaplan-Meier estimates of the survival curves by age and gender combination. The four panels correspond to females younger than 75, females aged 75 or older, males younger than 75 and males aged 75 or older.

Figure 2.5. Kaplan-Meier Estimates for Age and Gender Subgroups (Combined On-Drug Analysis)



2.4.3 Mortality Incidence Rate

The incidence rate is defined as a ratio with the number of events as the numerator and the total person-years at risk as the denominator. It is the average hazard over the follow up period. The incidence for each combination subgroup is given in Table 2.4.2. Note here the incidence was for the mixed patient population.

Table 2.4.2. Incidence Rate By Subgroup (Combined On-Drug Analysis)

Incidence rate (number of events / person-years follow up)	MK-0966	Placebo
Female, Age < 75	0.0052 (1/191)	0.0000 (0/200)
Female, Age 75 Years or Older	0.0140 (4/285)	0.0106 (3/284)
Male , Age < 75	0.0070 (3/426)	0.0060 (3/497)
Male , Age 75 Years or Older	0.0346 (14/405)	0.0067 (3/446)
Incidence rate in events per person-year follow up		

Incidence Rate For Each Gender And Age Category From Combined On-Drug Analysis