BRISTOL-MYERS SQUIBB COMPANY

IPILIMUMAB

Final Clinical Study Report for Study CA184124

SYNOPTIC REPORT

A RANDOMIZED, OPEN-LABEL, PHASE 2 SAFETY AND EFFICACY TRIAL OF IPILIMUMAB VERSUS PEMETREXED IN SUBJECTS WITH RECURRENT/STAGE IV NON-SQUAMOUS, NON-SMALL CELL LUNG CANCER WHO HAVE NOT PROGRESSED AFTER FOUR CYCLES OF A PLATINUM-BASED FIRST LINE CHEMOTHERAPY

Indication:	Non-small cell lung cancer
Phase:	2
Study Initiation Date:	11-Jul-2012
Study Completion Date:	25-Feb-2013
Report Date:	18-Dec-2013
Document Control Number:	930075859
Previous Version(s) of this Report:	None

THIS STUDY WAS CONDUCTED IN ACCORDANCE WITH GOOD CLINICAL PRACTICE

Sponsor's Responsible Medical Officer:
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SYNOPSIS

Final Clinical Study Report for Study CA184124

TITLE OF STUDY: A Randomized, Open-Label, Phase 2 Safety and Efficacy Trial of Ipilimumab versus Pemetrexed in Subjects with Recurrent/Stage IV Non-Squamous, Non-Small Cell Lung Cancer Who Have Not Progressed After Four Cycles of a Platinum-Based First Line Chemotherapy

PURPOSE: CA184124 was designed to compare the efficacy and safety of ipilimumab to pemetrexed when administered as a maintenance/switch-maintenance therapy in subjects with non-small cell lung cancer (NSCLC). The primary endpoint was overall survival (OS).

After only 9 subjects had been enrolled, the study was terminated for administrative reasons unrelated to any adverse events (AEs) or expectation of efficacy associated with either ipilimumab or pemetrexed. This synoptic report presents complete safety results for all treated subjects. Individual results for OS are also presented with no formal summary or comparison between the treatment arms due to the limited number of subjects enrolled in the study.

NUMBER OF SUBJECTS: Enrollment of approximately 250 subjects was planned, 9 subjects were enrolled, 8 subjects were treated and all 8 subjects went off-treatment due to disease progression (6), death (1) or study drug toxicity (1).

DISPOSITION, DEMOGRAPHICS AND OTHER PERTINENT BASELINE CHARACTERISTICS:

Subject disposition, baseline demographic and disease characteristics are presented in the following tables.

	Number of Subjects (%)			
	10 mg/kg Ipilimumab N=6	**500 mg/m^2 Pemetrexed N=2**	**Not Randomized N=1**	**Total N=9**
Number of enrolled subjects	6	2	1	9
Number randomized	6 (100.0)	2 (100.0)	0	8 (88.9)
Number not randomized	0	0	1 (100.0)	1 (11.1)
Number treated	6 (100.0)	2 (100.0)	0	8 (88.9)
Number not treated	0	0	1 (100.0)	1 (11.1)
Reason not treated				
Disease progression	0	0	1 (100.0)	1 (11.1)
Number off treatment	6 (100.0)	2 (100.0)	-	8 (100.0)[a]
Reason off treatment				
Disease progression	4 (66.7)	2 (100.0)	-	6 (75.0) [a]
Death	1 (16.7)	0	-	1 (12.5) [a]
Study drug toxicity	1 (16.7)	0	-	1 (12.5) [a]

[a] percentages are calculated based on number of treated subjects

Demography and Subject Characteristics-Randomized Subjects

	10 mg/kg Ipilimumab N=6	500 mg/m^2 Pemetrexed N=2	Total N=8
Age (years)			
Mean (SD)	62.7 (8.85)	61.0 (1.41)	62.3 (7.54)
Min, Max	49-76	60-62	49-76
<65	4 (66.7)	2 (100.0)	6 (75.0)
≥65	2 (33.3)	0	2 (25.0)
Gender (%)			
Male	4 (66.7)	1 (50.0)	5 (62.5)
Female	2 (33.3)	1 (50.0)	3 (37.5)
Race (%)			
White	6 (100.0)	2 (100.0)	8 (100.0)
Baseline ECOG PS			
0	3 (50.0)	1 (50.0)	4 (50.0)
1	3 (50.0)	1 (50.0)	4 (50.0)
Baseline disease stage at study entry			
Stage IV	6 (100.0)	2 (100.0)	8 (100.0)

ECOG PS: Eastern Cooperative Oncology Group performance status, SD: standard deviation

SUMMARY OF RESULTS:

OVERALL SURVIVAL:

A total of 2 (33.3%) subjects in the 10 mg/kg ipilimumab arm died. No deaths were reported in the pemetrexed arm. The OS for the ipilimumab arm ranged between 0.9 and 4.6+ months and for the pemetrexed arm was 5.4+ months.

SAFETY:

- Deaths were reported in 2 (33.3%) subjects treated with 10 mg/kg ipilimumab; one due to arterial injury and the other due to acute myocardial infarction. The investigator assessed both the deaths to be not related to study treatment. No deaths were reported in subjects treated with 500 mg/m^2 pemetrexed.
- Treatment-related serious adverse events (SAEs) were reported in 3 (50%) subjects treated with 10 mg/kg ipilimumab and included colitis, hypopituitarism, and urticaria in one subject each.
- Adverse events leading to discontinuation were reported in 1 (16.7%) subject treated with 10 mg/kg ipilimumab and none in subjects treated with 500 mg/m^2 pemetrexed.
- Common AEs (reported in at least 4 subjects) in the 10 mg/kg ipilimumab arm were (in decreasing frequency) rash, diarrhea, decreased appetite, asthenia, and fatigue; common AEs in the 500 mg/m^2 pemetrexed arm were anemia, pyrexia, bronchitis, and fracture.

A summary of the safety results is presented in the following table.

Overall Safety Summary-All Treated Subjects

	Number of Subjects (%)		
	10 mg/kg Ipilimumab N=6	**500 mg/m^2 Pemetrexed N=2**	**Total N=8**
Deaths - total	2 (33.3)	0	2 (25.0)
Within 30 days of last dose	1 (16.7)	0	1 (12.5)
Within 32 days of last dose date	1 (16.7)	0	1 (12.5)
Treatment-related SAEs	3 (50.0)	0	3 (37.5)
AEs leading to discontinuation	1 (16.7)	0	1 (12.5)
Experienced at least one AE	6 (100.0)	2 (100.0)	8 (100.0)

SAE: Serious adverse event

CONCLUSIONS:

- The study was terminated prior to reaching the enrollment goal after only 8 subjects were randomized. Conclusions on efficacy cannot be made due to the limited sample size.
- The most common toxicities for ipilimumab 10 mg/kg were as previously reported. No new types of AEs were observed.
- On study adverse events (AEs) leading to discontinuation were reported in 1 (16.7%) subject in Arm A (ipilimumab arm) and none in Arm B. The AE that led to discontinuation was grade 3 urticaria, assessed by the investigator as related to study treatment.
- There were no drug-related deaths on either arm.
- Treatment-related SAEs and AEs were consistent with the previously characterized immune-based toxicity profile of ipilimumab.

DATE OF REPORT: 18-Dec-2013