Rapport og sluttmelding Skjema for løpende rapport eller sluttmelding til de regionale komiteer for medisinsk og helsefaglig forskningsetikk (REK)

2010/2695-25
Dokument-id: 510513 Dokument mottatt 23.04.2015

En randomisert dobbeltblind fase 3-studie av docetaxel og ramucirumab versus docetaxel og placebo i behandlingen av ikke-småcellet lungekreft i stadium IV etter sykdomsprogresjon etter én tidligere platinabasert behandling (2010/2695)

1. Generelle opplysninger

a. Prosjektleder

Navn:	Odd Terje Brustugun
Akademisk grad:	Dr. med.
Klinisk kompetanse:	Spesialist onkologi
Stilling:	Overlege
Arbeidssted:	Oslo Universitetssykehus
Arbeidsadresse:	Montebello
Postnummer:	0310
Sted:	Oslo
Telefon:	22934000
E-post adresse:	otr@radiumhospitalet.no

b. Prosjekt

Hvilket prosjekt gjelder sluttmeldingen/rapporten?	En randomisert dobbeltblind fase 3-studie av docetaxel og ramucirumab versus docetaxel og placebo i behandlingen av ikke-småcellet lungekreft i stadium IV etter

2. Sluttmelding/rapport og etisk vurdering

Sluttmelding

Kortfattet, allment forståelig framstilling av prosjektets konklusjoner. Dette gjelder både positive og negative funn.

The primary objective of the JVBA (REVEL) study was to compare the overall survival (OS) of ramucirumab administered in combination with docetaxel versus placebo with docetaxel in patients with Stage IV NSCLC who had disease progression during or after 1 prior first-line platinum-based chemotherapy for advanced/metastatic disease. REVEL is the first study to demonstrate a statistically and clinically meaningful improvement in OS for a novel agent in combination with a standard chemotherapy in advanced NSCLC patients with progression after platinum-based chemotherapy. Consistent survival benefit was observed in both squamous and nonsquamous patients. The study met its primary endpoint, with a significant improvement in median survival of 1.4 months, and a 14.3% reduction in the risk of death (HR = 0.857; 95% CI: 0.751, 0.979; p=0.024) in patients treated with ramucirumab plus docetaxel compared to placebo plus docetaxel. Treatment with ramucirumab plus docetaxel significantly reduced the risk of disease progression or death by 23.8% compared with placebo plus docetaxel (HR = 0.762; p<0.001), and improved median PFS by 1.5 months in patients treated with ramucirumab plus docetaxel compared to placebo plus docetaxel. Statistically significant improvements in both ORR (22.9% vs. 13.6%,respectively; p<0.001) and DCR (64% vs. 52.6%, respectively; p<0.0001) were observed for the ramucirumab plus docetaxel arm over the placebo plus docetaxel arm. Subgroup analyses showed consistent results across multiple prespecified patient subgroups.

Ramucirumab in combination with docetaxel was well tolerated in the advanced NSCLC population, with manageable side effects. Overall, the safety profile observed was consistent with the safety profile for ramucirumab established in previous pivotal studies in gastric cancer, as well as the established safety profile for docetaxel. The results of REVEL represent a significant new second-line therapeutic option for patients with locally advanced or metastatic NSCLC with progression after platinum-based chemotherapy.

Kortfattet redegjørelse for gjennomføringen av prosjektet i forhold til opprinnelig søknad og plan for gjennomføring.

REVEL was a randomized, double-blind, global Phase 3 study conducted at 216 study centers across 26 countries. The study was initiated, executed, and completed according to planned study timelines. Planned enrollment was 1242 patients over a period of 26 months. Actual enrollment was 1253 patients (628 patients in Ramucirumab + Docetaxel arm and 625 patients in Placebo +

Docetaxel arm) randomized over a period of 26 months: the first patient enrolled on 03 December 2010 with the last patient entered study treatment on 04 February 2013. Statistical evaluation of key study endpoints was performed according to plan and as defined in the study protocol and statistical analysis plan. The primary efficacy analysis was performed on the ITT population, comparing Overall Survival (OS) between the 2 treatment arms when at least 869 death events were observed on the study. Key secondary endpoints including PFS, ORR, DCR, and evaluation of safety were also performed at the time of the primary analysis. An IDMC was established prior to enrollment of the first patient in the trial. The IDMC reviewed unblinded interim analyses of safety and efficacy data and these reviews were conducted as defined in the study protocol. There were 5 protocol amendments implemented throughout the study. Beginning with the 4th Protocol Amendment, the IDMC recommended a lower starting dose of docetaxel, 60 mg/m2 , for new patients enrolling in Korea and Taiwan.

3. Vedlegg

#	Type	Filnavn	Lagt inn dato
1.	Øvrige vedlegg	03 LY3009806 (IMC-1121B) IB Version 11.0_13May2014.pdf	22.04.15
2.	Øvrige vedlegg	02 LY3009806 (IMC-1121B) IB Version 10.0_08Jul2013.pdf	22.04.15
3.	Øvrige vedlegg	00 I4T-MC-JVBA_EC_Cover letter(Transition+CSR+IB)_NO_22Apr2015.pdf	22.04.15
4.	Sluttmelding / publikasjon	01 I4T-MC-JVBA CSR synopsis 12Jun2014.pdf	22.04.15

4. Ansvarserklæring

Jeg erklærer at prosjektet vil bli gjennomført
I henhold til gjeldende lover, forskrifter og retningslinjer
I samsvar med opplysninger gitt i denne søknaden
I samsvar med eventuelle vilkår for godkjenning gitt av REK