A Randomised, Parallel, Double Blinded Study to Compare the Efficacy and Safety of FKB238 to Avastin® In 1st Line Treatment for Patients with Advanced/Recurrent Non-Squamous Non-Small Cell Lung Cancer in Combination of Paclitaxel and Carboplatin

Registry ID: PHRR160823-001347
Secondary Identification Number: FKB238-002; 2016-CT0356

UNIQUE URL


SCIENTIFIC TITLE

A Randomised, Parallel, Double Blinded Study to Compare the Efficacy and Safety of FKB238 to Avastin® In 1st Line Treatment for Patients with Advanced/Recurrent Non-Squamous Non-Small Cell Lung Cancer in Combination of Paclitaxel and Carboplatin

PROJECT DESCRIPTION

This is a global multi-centre, double-blind, parallel, Phase 3 study designed to compare the efficacy and safety of FKB238 and EU-Avastin when used in combination with paclitaxel and carboplatin in the 1st line treatment of advanced or recurrent NS-NSCLC.

NUHRA DETAILS

<table>
<thead>
<tr>
<th>NUHRA Regime</th>
<th>NUHRA Classification</th>
<th>NUHRA Priority</th>
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<tbody>
<tr>
<td>2010 - 2016</td>
<td>Health Technology Development</td>
<td>Drug Discovery and Development</td>
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PROJECT DURATION

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<tr>
<th>Start Date</th>
<th>Duration in Months</th>
<th>Target Completion Date</th>
<th>Actual Completion Date</th>
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<tbody>
<tr>
<td>2016-11-03</td>
<td>36</td>
<td>2019-11-03</td>
<td>0000-00-00</td>
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PROJECT STATUS

Ongoing

IMPLEMENTING AGENCY (PRIMARY SPONSOR)

<table>
<thead>
<tr>
<th>Name of Institution</th>
<th>Classification</th>
<th>Region</th>
<th>LTO #</th>
</tr>
</thead>
</table>

Contact #: (+632) 8377534, (+632) 8377537, (+632) 8372071-80 loc. 2117, 2112
Email: registry@pchrd.dost.gov.ph
**COOPERATING AGENCY (SECONDARY SPONSOR)**

<table>
<thead>
<tr>
<th>Name of Institution</th>
<th>Classification</th>
<th>Region</th>
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<tbody>
<tr>
<td>PAREXEL Clinical Research (Philippines) Ltd. Corp.</td>
<td>Private Business</td>
<td>NCR</td>
<td>CDRR-NCR-CRO-4</td>
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**FUNDING AGENCY (SOURCES OF MONETARY OR MATERIAL SUPPORT)**

1. Centus Biotherapeutics Limited

**CONTACT FOR PUBLIC QUERIES**

<table>
<thead>
<tr>
<th>Name:</th>
<th>Email Address:</th>
<th>Phone Number:</th>
<th>Postal Address:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cheryl Dy</td>
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<td>+632 988 6215</td>
<td>PAREXEL Clinical Research (Phil.), Ltd. Corp. 15th Floor, Philam Life Tower 8767 Paseo De Roxas Makati City, Philippines 1226</td>
</tr>
</tbody>
</table>

**CONTACT FOR SCIENTIFIC QUERIES**

<table>
<thead>
<tr>
<th>Name:</th>
<th>Email Address:</th>
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<tbody>
<tr>
<td>Maaliddin Biruar</td>
<td><a href="mailto:Maaliddin.Biruar@parexel.com">Maaliddin.Biruar@parexel.com</a></td>
<td>632 988 6201</td>
<td>PAREXEL Clinical Research (Philippines) Ltd. Corp 15F Philam Life Tower 8767 Paseo de Roxas, Makati City 1226 Philippines</td>
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**INVESTIGATING TEAM**

<table>
<thead>
<tr>
<th>Name</th>
<th>Expertise</th>
<th>Affiliation</th>
</tr>
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<tbody>
<tr>
<td>Roselle De Guzman, MD</td>
<td>Oncologist</td>
<td>St. Luke's Medical Center - Quezon City</td>
</tr>
<tr>
<td>Marie Cherry Lynn Samson-Fernando, MD</td>
<td>Oncologist</td>
<td>Manila Doctors Hospital</td>
</tr>
<tr>
<td>Arnold John Uson, MD</td>
<td>Oncologist</td>
<td>Perpetual Succour Hospital</td>
</tr>
<tr>
<td>Heinrik Martin Jude S. Strebel, MD</td>
<td>Oncologist</td>
<td>Philippine General Hospital</td>
</tr>
<tr>
<td>Jennifer Sandoval-Tan, MD</td>
<td>Oncologist</td>
<td>Philippine General Hospital</td>
</tr>
<tr>
<td>Maria Belen E. Tamayo, MD</td>
<td>Oncologist</td>
<td>Makati Medical Center</td>
</tr>
<tr>
<td>John P. Querol, MD</td>
<td>Oncologist</td>
<td>The Medical City</td>
</tr>
<tr>
<td>Necty Juat, MD</td>
<td>Oncologist</td>
<td>National Kidney and Transplant Institute</td>
</tr>
</tbody>
</table>
HEALTH CONDITION(S) OR PROBLEM(S) STUDIED
Advanced/Recurrent Non Squamous Non Small Cell Lung Cancer

PRIMARY OUTCOMES

efficacy equivalence of FKB238 and EU approved-Avastin (EU-Avastin) when used in combination with paclitaxel/carboplatin as measured by overall response rate (ORR)

KEY SECONDARY OUTCOMES
None

DATE OF FIRST ENROLLMENT
2016-11-03

RECRUITMENT STATUS
Recruiting

COUNTRIES OF RECRUITMENT
Unspecified

RESEARCH CLASSIFICATION
Clinical Trial

PROJECT LOCATION & INSTITUTIONAL ETHICS REVIEW BOARD WHICH APPROVED THE STUDY

<table>
<thead>
<tr>
<th>Project Location</th>
<th>Institutional Ethics Review Board</th>
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<tr>
<td>St. Luke’s Medical Center - Quezon City</td>
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<td>Manila Doctors Hospital</td>
<td>Manila Doctors Hospital Institutional Review Board</td>
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<tr>
<td>Perpetual Succour Hospital</td>
<td>Perpetual Succour Hospital Institutional Ethics and Review Board</td>
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<td>Philippine General Hospital</td>
<td>Philippine General Hospital Ethics Review Board</td>
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<td>The Medical City</td>
<td>The Medical City - Institutional Review Board</td>
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<tr>
<td>National Kidney and Transplant Institute</td>
<td>National Kidney and Transplant Institute Ethics Review Committee</td>
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Email: registry@pchrd.dost.gov.ph
FDA DOCUMENT TRACKING NUMBER
20160512120033

FDA / ERC APPROVAL DATE
2016-08-10

AMENDMENT APPROVAL DATES/REASONS

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<tr>
<th>Approval Date</th>
<th>Amendment Classification</th>
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<td>2016-08-15</td>
<td>Amendments related to the trial arrangements</td>
<td>Change of the trial site or addition of new site</td>
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<tr>
<td>2016-08-15</td>
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<td>Change of the principal investigator or addition of new ones</td>
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<td>2017-08-14</td>
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<td>Informed consent</td>
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<td>2018-09-28</td>
<td>Amendments related to the protocol</td>
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KEY INCLUSION AND EXCLUSION CRITERIA (CT)

Inclusion criteria:
1. Patients aged 18 years or older
2. Newly diagnosed advanced (stage IV) / recurrent NS-NSCLC for which they had not received any systemic anti-cancer therapy for metastatic disease, including chemotherapy, biologic therapy, immunotherapy, or any investigational drug
3. Histologically or cytologically confirmed diagnosis of predominantly NS-NSCLC
4. Be eligible to receive study treatment of bevacizumab, paclitaxel, and carboplatin for the treatment of advanced or recurrent NS-NSCLC
5. Existence of at least 1 measurable lesion by response evaluation criteria (RECIST v1.1), defined as; at least one lesion, not previously irradiated, that can be accurately measured at baseline as ≥ 10 mm in the longest diameter (except lymph nodes which must have short axis ≥ 15 mm) with computed tomography (CT) or magnetic resonance imaging (MRI) which is suitable for accurate repeated measurements.
6. Eastern Collaborative Oncology Group Performance Status (ECOG PS) 0 or 1
7. Life expectancy longer than 6 months
8. Adequate haematological function: absolute neutrophil count ≥ 1.5 × 10^9/L; platelets ≥ 100 × 10^9/L; haemoglobin ≥ 9 g/dL
9. International normalised ratio (INR) ≤ 1.5 and partial thromboplastin time ≤ 1.5 × the upper limit of normal (ULN) within 7 days prior to starting study treatment
10. Adequate liver function: Serum bilirubin ≤ 1.5 × ULN (and in case of documented Gilbert Syndrome [unconjugated hyperbilirubinaemia] ≤ 3 × ULN); transaminases ≤ 2.5 × ULN (and in case of liver metastases < 5 × ULN)
11. Adequate renal function:
a. Creatinine clearance, measured and/or calculated according to the formula of Cockroft and Gault ≥ 60 mL/min AND
b. Urine dipstick or urinalysis for proteinuria < 2+. If the urine dipstick or urinalysis is ≥ 2+, 24-hour urine must demonstrate ≤ 1 g of protein in 24 hours
12. Negative serum/urine pregnancy test within 7 days of starting study treatment in premenopausal women and women < 2 years after the onset of menopause
13. Signed informed consent
14. Able to comply with the protocol

Exclusion Criteria
1. Small cell lung cancer (SCLC) or combination SCLC and NSCLC. Squamous-cell tumours and mixed adenosquamous carcinomas of predominantly squamous nature
2. Recurrence occurred within 12 months from the last dose of neoadjuvant/adjuvant therapy
3. Any unresolved toxicities from prior systemic therapy (eg, adjuvant chemotherapy) greater than Common Terminology Criteria for Adverse Events (CTCAE) grade 1 at the time of starting study drug with the exception of alopecia
4. Evidence of a tumour that compresses or invades major blood vessels or tumour cavitation that in the opinion of the investigator is likely to bleed
5. Known sensitising EGFR mutations (eg, deletion 19 or L858R) or EML4-ALK translocation positive mutations
6. Previous dosing with vascular endothelial growth factor (VEGF) inhibitor
7. Brain metastasis or spinal cord compression (computed tomography or magnetic resonance imaging of the head is required within 4 weeks prior to randomisation)
8. Malignancy other than NS-NSCLC within 5 years before randomisation, except for adequately treated carcinoma in situ of the cervix, basal or squamous cell skin cancer, localised prostate cancer treated surgically with curative intent, or ductal carcinoma in situ of the breast treated surgically with curative intent
9. Known hypersensitivity to active ingredients or any excipients of the IPs and combination chemotherapy
10. Use of aspirin (> 325 mg/day) or treatment with dipyridamole, ticlopidine, clopidogrel, prasugrel, or cilostazol within 14 days before the first dose of IP
11. Use of full-dose oral or parenteral anticoagulants or thrombolytic agents within 6 months before the first dose of IP (use of low dose anticoagulants for venous access device maintenance or prophylactic use of anticoagulants will be allowed)
12. Known Hepatitis B, Hepatitis C, or human immunodeficiency virus (HIV) infection
13. Major surgery, significant traumatic injury, or radiotherapy (except for palliative intention which requires 14 days wash out period for bone lesions outside the thoracic region) within 28 days before the first dose of IP or anticipation of the need for major surgery during study treatment
14. Fine needle aspirations, indwelling catheter placement, or core biopsy within 7 days of randomisation
15. Non-healing wound, ulcer, or bone fracture
16. Uncontrolled hypertension or systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg
17. Patients with unstable angina, myocardial infarction, coronary artery bypass graft, angioplasty, vascular stenting, or cardiovascular event within 6 months before the first dose of IP; coagulopathy, any bleeding disorders, poorly controlled diabetes, or active gastrointestinal inflammation such as gastric or duodenal ulcer, diverticulitis, inflammatory bowel disease, or cholecystitis
18. History of fistulas or abdominal perforations
19. History of arterial or venous thromboembolic or ischemic events, or congestive heart failure (New York Heart Association class ≥ 2) within 6 months before the first dose of IP
20. History of haemoptysis of ≥ ½ teaspoon of red blood within 28 days before the first dose of IP
21. Fertile men or women of childbearing potential not using adequate contraception. Patients of child bearing potential and their partners, who are sexually active, must agree to the use of at least one highly effective form of contraception throughout their participation in the study and for 6 months after last dose of study treatment
22. Breastfeeding women (unless the patient is willing to discontinue breastfeeding throughout their...
participation in the study and for 6 months after last dose of study treatment)
23. Treatment with any other investigational agent for any reason, or within 28 days before the first dose of IP
24. Presence of any other disease, metabolic dysfunction, physical examination finding, or laboratory finding that, in the opinion of the investigator, puts the patient at high risk for treatment-related complications in this study

STUDY TYPE
Interventional

INTERVENTION NAME
FKB238-002

INTERVENTION DESCRIPTION
Intervention group:
FKB238 group: paclitaxel + carboplatin (combination drugs) + FKB238 (investigational product [IP])
Avastin group: paclitaxel + carboplatin (combination drugs) + EU-Avastin (IP)

METHOD OF ALLOCATION
Randomized

MASKING / BLINDING
Double Blind

MASKING DETAILS
None

ASSIGNMENT
Parallel

PURPOSE
To demonstrate the efficacy equivalence of FKB238 and EU approved-Avastin (EU-Avastin) when used in combination with paclitaxel/carboplatin as measured by overall response rate (ORR)

PHASE
Phase III

TARGET SAMPLE SIZE (PHILIPPINES)
72

ACTUAL SAMPLE SIZE (PHILIPPINES)
12

REASON FOR THE DIFFERENCE BETWEEN TARGET & ACTUAL SAMPLE SIZES
Unspecified

DATE OF FIRST ENROLLMENT
2016-11-03

RESEARCH UTILIZATION
None