An Open-label, Randomized Phase 3 Efficacy Study of ASP8273 vs Erlotinib or Gefitinib in First-line Treatment of Patients with Stage IIIB/IV Non-small Cell Lung Cancer Tumors with EGFR Activating Mutations

Published: 28-10-2015
Last updated: 19-04-2024

Primary• To evaluate the progression free survival (PFS), based on independent radiologic review (IRR), of ASP8273 compared to erlotinib or gefitinib in patients with locally advanced, metastatic or unresectable stage IIIB/IV adenocarcinoma non-...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON44112

Source
ToetsingOnline

Brief title
SOLAR

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
cancer, tumor

Research involving

Human

Sponsors and support

Primary sponsor: Astellas Pharma Global Development, Inc.
Source(s) of monetary or material Support: Sponsor is Astellas

Intervention

Keyword: Cancer, Tumor

Outcome measures

Primary outcome

Progression Free Survival

Secondary outcome

Secondary

• Overall survival (OS)

• Overall response rate (ORR)

• Progression Free Survival as assessed by the investigator

• Disease control rate (DCR)

• Duration of Response (DOR)

• Safety of ASP8273

• Evaluate Quality of Life (QoL) and patient-reported outcome (PRO) parameters

Study description

Background summary

Lung cancer is a leading cause of cancer death worldwide. Lung cancer accounts for over 1 million mortalities annually and NSCLC accounts for almost 85% of all cases [Esposito et al, 2010; Herbst et al, 2008; Ferlay et al, 2007].
Epidermal growth factor receptor (EGFR) mutations are found in approximately 10% and 30% of NSCLC patients in North American/ European and East Asian

countries, respectively [Bell et al, 2005; Shigematsu et al, 2005]. EGFR activating mutations result in increased malignant cell survival, proliferation, invasion, metastatic spread and tumor angiogenesis in NSCLC [Herbst et al, 2008; Mendelsohn & Baselga, 2000; Wells A, 1999].

ASP8273 mesilate is a novel, small molecule irreversible tyrosine kinase inhibitor (TKI) that inhibits the kinase activity of EGFR containing the exon 19 deletion (del ex19) or the exon 21 (L858R) substitution activating mutation as well as the T790M resistance mutation with higher potency than wild type EGFR.

Study objective

Primary
• To evaluate the progression free survival (PFS), based on independent radiologic review (IRR), of ASP8273 compared to erlotinib or gefitinib in patients with locally advanced, metastatic or unresectable stage IIIB/IV adenocarcinoma non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) activating mutations

Study design

Approximately 540 subjects will be randomized 1:1 to 1 of 2 treatment arms (Arm A or Arm B). Arm A will receive 300 mg daily of ASP8273 and Arm B will receive either 150 mg erlotinib or 250 mg gefitinib daily, as decided by the investigator prior to randomization. Both arms will follow 28-day cycles of continuous dosing.

Subjects will be allowed to receive ASP8273 or erlotinib/gefitinib until discontinuation criteria are met.

Intervention

The patient will receive ASP8237 or Erlotinib or Gefitinib

Study burden and risks

The initial safety observations from earlier trials are consistent with the preclinical findings and other approved EGFR TKI therapies. Therefore, the possible benefits of antitumor activity in subjects taking ASP8273 therapy appear to outweigh potential risks in this patient population. See the current ASP8273 Investigator*s Brochure for full list of TEAEs.

Erlotinib and Gefitinib both have well characterized safety profiles with acceptable management of AEs in the clinical setting.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Subject must meet all of the following inclusion criteria to be eligible for participation in this study at enrollment:;1. Institutional Review Board (IRB)/Independent Ethics Committee (IEC) approved written informed consent and privacy language as per national regulations (e.g., HIPAA Authorization for U.S. sites) must be obtained from the subject or legally authorized representative prior to any;study-related procedures.;2. Subject is >= 18 years of age and legally an adult according to local regulation at the time of signing informed consent.;3. Subject agrees not to participate in another interventional study while on treatment.;4. Female subject must either:;Be of nonchildbearing potential:;- postmenopausal (defined as at least 1 year without any menses) prior to Screening, or;- documented surgically sterile;Or, if of childbearing potential:;- Agree not to try to become pregnant during the study and for 28 days after the final study drug administration;- And have a negative serum pregnancy test at Screening;- And, if heterosexually active, agree to consistently use 2 forms of birth control*

(at least 1 of which must be a highly effective method* and one must be a barrier method) starting at Screening and throughout the study period and for 28 days after the final study drug administration;5. Female subject must not be breastfeeding at Screening or during the study period, and for 28 days after the final study drug administration.;6. Female subject must not donate ova starting at Screening and throughout the study period, and for 28 days after the final study drug administration.;7. Male subject and their female spouse/partners who are of childbearing potential must be using highly effective contraception consisting of 2 forms of birth control* (1 of which must be a barrier method) starting at Screening and continue throughout the study period and for 90 days after the final study drug administration.;*Highly effective forms of birth control include:;- Consistent and correct usage of established oral, injected or implanted hormonal methods of contraception;- Established intrauterine device (IUD) or intrauterine system (IUS);*Acceptable methods of birth control include:;- Barrier methods of contraception: condom or occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/film/cream/suppository.;8. Male subject must not donate sperm starting at Screening and throughout the study period and for 90 days after the final study drug administration.;9. Subject has Eastern Cooperative Oncology Group (ECOG) performance status <= 2.;10. Subject has histologically confirmed locally advanced, metastatic or unresectable Stage IIIB/IV adenocarcinoma NSCLC (newly diagnosed or recurrent). Subjects with mixed histology are eligible if adenocarcinoma is the predominant histology.;11. Subject has predicted life expectancy >= 12 weeks in the opinion of the investigator.;12. Subject must meet all of the following criteria on the laboratory tests that will be analyzed centrally within 7 days prior to the first dose of study drug. In case of multiple laboratory data within this period, the most recent data should be used.;- Neutrophil count > 1,000/mm^3;- Platelet count >= 7.5 x 10^4 /mm^3;- Hemoglobin > 8.0 g/dL;- Serum creatinine < 2.0 x upper limit of normal (ULN) or an estimated glomerular filtration rate (eGFR) of > 50 mL/min as calculated by the Cockcroft Gault Method;Total bilirubin < 1.5 x ULN (except for subjects with documented Gilbert*s syndrome);AST and ALT < 3.0 x ULN or <= 5 x ULN if subject has documented liver metastases;Serum sodium level is >= 130 mmol/L;13. Subject has an EGFR activating mutation (exon 19 deletion or exon 21 L858R), with or without T790M mutation, by local or central testing on examination of a NSCLC FFPE specimen (archival or fresh biopsy). Subjects harboring both exon 19 deletion and exon 21 L858R mutations are not eligible. A tissue sample from the same block used to determine eligibility by local testing should be available to send to the central lab for confirmatory testing. Subjects randomized based on local results indicating presence of EGFR mutation may remain on study if central results are discordant.;14. Subject must have at least 1 measureable lesion based on RECIST V1.1. Previously irradiated lesions will not be considered as measurable lesions.

Exclusion criteria

Subject who meets any of the following exclusion criteria prior to enrollment is not eligible for enrollment:;1. Subject has received intervening anticancer treatment or previous treatment with chemotherapy;for metastatic disease other than palliative local radiation to painful bone metastases completed at least 1 week prior to the first dose of study drug. The administration of neoadjuvant or adjuvant chemotherapy is allowed as long as it has finalized

>= 6 months before the first dose of study drug.;2. Subject has received a prior treatment with a therapeutic agent targeting EGFR (e.g., afatinib, dacomitinib, ASP8273, etc).;3. Subject has received investigational therapy within 28 days or 5 half-lives prior to the first dose of study drug.;4. Subject has received radiotherapy within 1 week prior to the first dose of study drug. If the subject received radiotherapy > 1 week prior to study treatment, the irradiated lesion cannot be the only lesion used for evaluating response.;5. Subject has symptomatic central nervous system (CNS) metastasis. Subject with previously treated brain or CNS metastases are eligible provided that the subject has recovered from any acute effects of radiotherapy, does not have brain metastasis related symptoms, is not requiring systemic steroids for at least 2 weeks prior to study drug administration, and any whole brain radiation therapy was completed at least 4 weeks prior to study drug administration, or any stereotactic radiosurgery (SRS) was completed at least 2 weeks prior to study drug administration. Steroid inhaler use or ointment treatment for other concomitant medical disease is permitted.;6. Subject has received blood transfusions or hematopoietic factor therapy within 14 days prior to the first dose of study drug.;7. Subject has had a major surgical procedure (other than a biopsy) within 14 days prior to the first dose of study drug, or one is planned during the course of the study.;8. Subject has a known history of a positive test for human immunodeficiency virus (HIV) infection.;9. Subject has known history of serious hypersensitivity reaction to a known ingredient of ASP8273, erlotinib or gefitinib.;10. Subject has evidence of an active infection requiring systemic therapy within 14 days prior to the planned first dose of study drug.;11. Subject has severe or uncontrolled systemic diseases including uncontrolled hypertension (blood pressure > 150/100 mmHg) or active bleeding diatheses.;12. Subject has history of drug-induced interstitial lung disease (ILD) or any evidence of active ILD.;13. Subject has ongoing cardiac arrhythmia that is Grade >= 2 or uncontrolled atrial fibrillation of any;grade.;14. Subject currently has Class 3 or 4 New York Heart Association congestive heart failure.;15. Subject has history of severe/unstable angina, myocardial infarction or cerebrovascular accident within 6 months prior to the planned first dose of study drug.;16. Subject has history of gastrointestinal ulcer or gastrointestinal bleeding within 3 months prior to the planned first dose of study drug.;17. Subject has concurrent corneal disorder or any ophthalmologic condition which, in the investigator*s opinion, makes the subject unsuitable for study participation (i.e., advanced cataracts, glaucoma).;18. Subject has difficulty taking oral medication or any digestive tract dysfunction or inflammatory bowel disease that would interfere with the intestinal absorption of drug.;19. Subject has another past or active malignancy which requires treatment. Prior carcinoma in situ or non-melanoma skin cancer after curative resection are permitted.;20. Subject has any condition which, in the investigator*s opinion, makes the subject unsuitable for study participation.;21. Subject has received potent CYP 3A4 inhibitors within 7 days prior to first dose of study drug or proton pump inhibitors such as omeprazole within 14 days prior to first dose of study drug.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-12-2016
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ASP8273
Generic name:	ASP8273
Product type:	Medicine
Brand name:	Iressa
Generic name:	gefitinib
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Tarceva
Generic name:	erlotinib
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	28-10-2015
Application type:	First submission

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-03-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-03-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-05-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-09-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-11-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-01-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-03-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-04-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-05-2017
Application type:	Amendment

Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	14-06-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	13-10-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2015-002894-39-NL
ClinicalTrials.gov	NCT02588261
CCMO	NL55228.091.15

Study results

Results posted: 25-10-2018

First publication
01-01-1900