A Randomized, Open-label, Phase 3 Study Comparing Once-weekly vs Twice-weekly Carfilzomib in Combination with Lenalidomide and Dexamethasone in Subjects With Relapsed or Refractory Multiple Myeloma (A.R.R.O.W.2)

Published: 08-01-2019
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Primary Objective: • To compare efficacy of once-weekly KRd (56 mg/m2) to twice-weekly KRd (27 mg/m2) in subjects with RRMM with 1 to 3 prior lines of therapyKey Secondary Objectives: • To compare progression-free survival (PFS) between treatment...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON52761

Source
ToetsingOnline

Brief title
20180015

Condition

- Other condition

Synonym
A form of bone marrow cancer, cancer of plasma cells

Health condition

bloedcel kanker

Research involving
Human

Sponsors and support

Primary sponsor: Amgen
Source(s) of monetary or material Support: Amgen

Intervention

Keyword: Carfilzomib, One weekly vs Twice-weekly, Open-Label, Relapsed Multiple Myeloma

Outcome measures

Primary outcome

overall response, defined as the best overall response of stringent complete response [sCR], complete response [CR], very good partial response [VGPR], and partial response [PR] per International Myeloma Working Group Uniform Response Criteria [IMWG-URC]) over the duration of the study

Secondary outcome

- PFS over the duration of the study

- convenience as measured by the Patient-reported Convenience With Carfilzomib-dosing Schedule Question after cycle 4 of treatment

- incidence of treatment-emergent adverse events

- time to response (TTR)

- duration of response (DOR)

- time to progression (TTP)

- MRD[-]CR , defined as achievement of CR or better by Independent Review Committee (IRC) per IMWG-URC and achievement of MRD negativity as assessed by next-generation sequencing method at a 10-5 threshold over the duration of the

study

- MRD[-] status at 12 months, defined as achievement of MRD negativity at 12 months (± 4 weeks) from randomization, as assessed by next-generation sequencing method at a 10-5 threshold

- physical functioning and role functioning over time as measured by the Physical Functioning and Role Functioning scales of the European Organization for Research and Treatment of Cancer Quality-of-life Questionnaire Core 30 (EORTC QLQ-C30) over the duration of the study

- treatment satisfaction as measured by the Satisfaction With Therapy (SWT) scale of the Cancer Therapy Satisfaction Questionnaire (CTSQ) after cycle 4 of treatment

Study description

Background summary

Multiple myeloma, a clonal neoplastic proliferation of plasma cells, is the second most common hematologic malignancy and is responsible for approximately 80 000 annual deaths worldwide (1% of all cancer deaths). The estimated incidence of multiple myeloma worldwide was 114 000 patients, which represents 0.8% of all cancers. The 5-year prevalence of multiple myeloma worldwide was estimated 229 000 persons (Ferlay et al, 2015). Multiple myeloma is a disease of older adults, with a median age at diagnosis of 69 years (Noone et al, 2018). As the world*s older population (age > 65 years) continues to grow (from 8.5% [617 million] of the world*s population in 2013 to a projected 17% [1.6 billion] in 2015) (He et al, 2016), the incidence of multiple myeloma is expected to increase.

Study objective

Primary Objective:
• To compare efficacy of once-weekly KRd (56 mg/m2) to twice-weekly KRd (27 mg/m2) in subjects with RRMM with 1 to 3 prior lines of therapy

Key Secondary Objectives:
• To compare progression-free survival (PFS) between treatment arms
• To compare patient-reported convenience with carfilzomib dosing schedule between treatment arms

Kindly refer to protocol section 4 for more information on Objectives and additional secondary objectives and endpoints.

Study design

The study will consist of a screening period of up to 28 days, a treatment duration of up to 12 cycles of 28 days, a 30-day safety follow-up period, and a long-term follow-up (every 28 +-7 days) period.
Subjects will receive the study drug(s) determined by randomization for a maximum of 12 cycles. No crossover between the treatment arms is allowed.

Upon discontinuation from the study treatment for any reason, a safety follow-up visit will be performed approximately 30 (+3) days after the last dose of all study drug(s). After discontinuation from study treatment, subjects who do not have confirmed PD are required to continue follow-up every 28 ± 7 days for survival. After end of study, subjects may continue treatment per local standard of care at the discretion of the investigator.

Subjects will be randomized in a 1:1 ratio to 1 of 2 arms:
Arm 1: KRd using once-weekly carfilzomib 56 mg/m2
Arm 2: KRd using twice-weekly carfilzomib 27 mg/m2

The overall study design is outlined in the study schema in Section 2.1 of the protocol.

Intervention

n/a

Study burden and risks

See E9 and E9a

Contacts

Public
Amgen

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NL
Scientific
Amgen

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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 has multiple myeloma with documented relapse or progression after most recent myeloma treatment.
• Subjects must have at least PR to at least 1 line of prior therapy
• Subjects must have received at least 1 but not more than 3 prior lines of therapy for multiple myeloma (induction therapy followed by stem cell transplant and consolidation maintenance therapy will be considered as 1 line of therapy).
• Prior therapy with a PI is allowed if the patient achieved at least a PR to most recent treatment with a PI, did not relapse within 60 days of discontinuation of the PI and the PI was not removed due to toxicity. A history of prior neuropathy is permitted if this was not grade 3, grade 4 or grade 2 with pain and if not resolved within the 14 days before enrollment, is less than or equal to grade 2 without pain.
• Eastern Cooperative Oncology Group Performance Status (ECOG PS) of < 2

Please refer to section 6.1 of the protocol.

Exclusion criteria

• Waldenström macroglobulinemia
• Multiple myeloma of IgM subtype
• Active congestive heart failure (New York Heart Association [NYHA] Class III to IV), symptomatic ischemia, uncontrolled arrhythmias, ECG abnormalities, pericardial disease, or myocardial infarction within 4 months prior to enrollment
• Uncontrolled hypertension

Please refer to section 6.2 of the protocol.

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):	03-09-2019
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Kyprolis
Generic name:	Carfilzomib
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	08-01-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-05-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-12-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-02-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-11-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-12-2020

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-06-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-07-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-10-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-12-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-12-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-02-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-06-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-09-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2018-000665-36-NL
ClinicalTrials.gov	NCT03859427
CCMO	NL68271.029.18

Study results