ARROW2

A Study Comparing Once-weekly vs Twice-weekly Carfilzomib in Combination With Lenalidomide and Dexamethasone in Subjects With Relapsed or Refractory Multiple Myeloma

NCT-Nummer:
NCT03859427

Studienbeginn:
Mai 2019

Letztes Update:
15.04.2021

Wirkstoff:
Carfilzomib, Lenalidomide, Dexamethasone
Indikation (Clinical Trials):
Multiple Myeloma, Neoplasms, Plasma Cell

Geschlecht:
Alle

Altersgruppe:
Erwachsene (18+)

Phase:
Phase 3

Sponsor:
Amgen

Collaborator:
-

Studien-Informationen

Brief Summary:

Compare efficacy of 56 mg/m2 carfilzomib administered once-weekly in combination with lenalidomide and dexamethasone (KRd 56 mg/m2) to 27 mg/m2 carfilzomib administered

twice-weekly in combination with lenalidomide and dexamethasone (KRd 27 mg/m2) in subjects with relapsed or refractory multiple myeloma (RRMM) with 1 to 3 prior lines of therapy.

Ein-/Ausschlusskriterien

Inclusion Criteria:

Documented relapse or progressive multiple myeloma after last treatment. Subjects refractory to the most recent line of therapy are eligible, unless last treatment contained PI or lenalidomide and dexamethasone). Refractory is defined as disease that is nonresponsive or progresses within 60 days of last therapy.

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 or the combination of lenalidomide and dexamethasone are allowed, if, the patient had at least a PR to the most recent therapy with a PI or lenalidomide and dexamethasone, neither PI or lenalidomide and dexamethasone in combination were ceased due to toxicity (unless at the time of enrollment that toxicity was neuropathy not exceeding grade 2 which has either resolved or if ongoing is less than or equal to grade 1), the patient has not received a PI and has not received lenalidomide and dexamethasone in combination in the 6 months prior to first study treatment. (Patients are permitted to have received single agent lenalidomide as maintenance therapy during the 6 months prior to first treatment)

Previous treatment with a lenalidomide and dexamethasone containing regimen is allowed, as long as the subject did not progress during the first 3 months after initiating lenalidomide and dexamethasone containing therapy.

Measurable disease with at least 1 of the following assessed within 21 days prior to

randomization:

- Inmunoglobulin G (IgG) multiple myeloma: serum monoclonal protein (M-protein) level ≥ 1.0 g/dL

- Inmunoglobulin A (IgA), Inmunoglobulin D (IgD), Inmunoglobulin E (IgE) multiple myeloma: serum M-protein level ≥ 0.5 g/dL

- Urine M-protein ≥ 200 mg per 24 hours

- In subjects without measurable serum or urine M-protein, serum-free light chain (SFLC) ≥ 100 mg/L (involved light chain) and an abnormal serum kappa lambda ratio

Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0 ≤ 2

Other inclusion criteria may apply

Exclusion Criteria:

Waldenström macroglobulinemia.

Multiple myeloma of Inmunoglobulin M (IgM) subtype.

Plasma cell leukemia (> 2.0 × 10^9 /L circulating plasma cells by standard differential).

Uncontrolled hypertension, defined as a subject whose blood pressure exceeds ≥ 160 mmHg systolic or ≥ 100 mmHg diastolic when taken in accordance with the European Society of Hypertension/European Society of Cardiology 2018 guidelines.

Active congestive heart failure (New York Heart Association Class III to IV), symptomatic ischemia, uncontrolled arrhythmias, screening ECG with corrected QT interval (QTc) of > 470 msec, pericardial disease, or myocardial infarction within 4 months prior to randomization.

Calculated or measured creatinine clearance < 1.0 mL/s (calculation must be based on the Cockcroft and Gault formula) within 21 days prior to randomization.

Other exclusion criteria may apply

Studien-Rationale

Primary outcome:

1. Overall Response Rate (ORR) (Time Frame - Through study completion, an average of 14 months):
ORR defined as the proportion of 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]

Secondary outcome:

1. Progression free survival (PFS) (Time Frame - Through study completion, an average of 14 months)

2. Convenience (Time Frame - Through study completion, an average of 14 months):
As measured by the Patient-reported convenience with carfilzomib dosing schedule question

3. Subject incidence of treatment-emergent adverse events (Time Frame - Through study completion, an average of 14 months)

4. Additional efficacy parameter - Time to Response (Time Frame - Through study completion, an average of 14 months):
As measured by Time to Response (TTR)

5. Additional efficacy parameter - Duration of Response (Time Frame - Through study completion, an average of 14 months):
Duration of Response (DOR)

6. Additional efficacy parameter - Time to Progression (Time Frame - Through study completion, an average of 14 months):
Time to Progression (TTP)

7. Overall Survival (Time Frame - Through study completion, an average of 14 months)

8. MRD[-]CR rate (Time Frame - Through study completion, an average of 14 months):
Defined as achievement of CR or better by Independent Review Committee (IRC) per IMWG-URC and achievement of Minimal Residual Disease (MRD) negativity as assessed by next-generation sequencing method at a 10^ -5 threshold

9. MRD[-] rate at 12 months (Time Frame - 12 months):
Defined as achievement of Minimal Residual Disease (MRD) negativity at 12 months (+/- 2 weeks) from randomisation as assessed by next-generation sequencing method at a 10^ -5 threshold

10. Physical functioning and role functioning (Time Frame - Through study completion, an average of 14 months):
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), a 30-item generic instrument for use in cancer subjects across tumor types

11. Treatment satisfaction as measured by the Satisfaction with Therapy (SWT) subscale of the Cancer Therapy Satisfaction Questionnaire (CTSQ) (Time Frame - 4 months):
Cancer Therapy Satisfaction Questionnaire (CTSQ) - measures treatment satisfaction in individuals with cancer

Studien-Arme

- Active Comparator: Carfilzomib once-weekly
  Carfilzomib, lenalidomide, dexamethasone (KRd) regimen using once-weekly carfilzomib 56 mg/m2
- Active Comparator: Carfilzomib twice-weekly
  Carfilzomib, lenalidomide, dexamethasone (KRd) regimen using twice-weekly carfilzomib 27 mg/m2

Geprüfte Regime

- Carfilzomib:
  Once weekly IV over 30 minutes on day 1, 8 and 15 of each 28 day cycle. The dose will be 20 mg/m2 on cycle 1 day 1 and 56 mg/m2 beginning with cycle 1 day 8 and thereafter. 12 cycles or until progression, unacceptable toxicity, death, loss to follow up or withdrawal of consent.
- Carfilzomib:
  Twice weekly IV over 10 minutes on day 1, 2, 8, 9, 15 and 16 of each 28 day cycle. The dose will be 20 mg/m2 on cycle 1 days 1 and 2 and 27 mg/m2 beginning with cycle 1 day 8 and thereafter. 12 cycles or until progression, unacceptable toxicity, death, loss to follow up or withdrawal of consent.
- Lenalidomide:
  Once daily orally 25 mg days 1 to 21 of each cycle. 12 cycles or until progression, unacceptable toxicity, death, loss to follow up or withdrawal of consent
- Dexamethasone:
  Once daily orally or by IV 40 mg days 1, 8 and 15 of each cycle. Also day 22 of cycles 1 to 9. 12 cycles or until progression, unacceptable toxicity, death, loss to follow up or withdrawal of consent

Studienleiter

MD
Study Director
Amgen

Kontakt

Amgen Call Center
Kontakt:
Phone: 866-572-6436
E-Mail: medinfo@amgen.com

Studienlocations (3 von 107)

Research Site
92708 Fountain Valley
United States

Status: Abgeschlossen

Research Site
80218 Denver
United States

Status: Abgeschlossen

Research Site
06062 Plainville
United States

Status: Abgeschlossen

Research Site
32207 Jacksonville
United States

Status: Abgeschlossen

Research Site
60068 Park Ridge
United States

Status: Abgeschlossen

Research Site
12208 Albany
United States

Status: Abgeschlossen

Research Site
45242 Cincinnati
United States

Status: Rekrutierend

Research Site
76201 Denton
United States

Status: Abgeschlossen

Research Site
76177 Fort Worth
United States

Status: Rekrutierend

Research Site
77030 Houston
United States

Status: Abgeschlossen

Research Site
78229 San Antonio
United States

Status: Abgeschlossen

Research Site
77380 The Woodlands
United States

Status: Rekrutierend

Research Site
5020 Salzburg
Austria

Status: Rekrutierend

Research Site
4002 Plovdiv
Bulgaria

Status: Rekrutierend

Research Site

1431 Sofia
Bulgaria

Status: Rekrutierend

Research Site
1756 Sofia
Bulgaria

Status: Rekrutierend

Research Site
625 00 Brno
Czechia

Status: Rekrutierend

Research Site
500 05 Hradec Kralove
Czechia

Status: Rekrutierend

Research Site
775 20 Olomouc
Czechia

Status: Rekrutierend

Research Site
128 08 Praha 2
Czechia

Status: Rekrutierend

Research Site
00290 Helsinki
Finland

Status: Rekrutierend

Research Site
90220 Oulu

Finland

Status: Rekrutierend

Research Site
20521 Turku
Finland

Status: Rekrutierend

Research Site
44000 Nantes
France

Status: Rekrutierend

Research Site
06202 Nice cedex 3
France

Status: Rekrutierend

Research Site
75010 Paris
France

Status: Rekrutierend

Research Site
75013 Paris
France

Status: Rekrutierend

Research Site
69495 Pierre-Benite
France

Status: Rekrutierend

Research Site
86021 Poitiers Cedex
France

Status: Rekrutierend

Research Site
35033 Rennes
France

Status: Rekrutierend

Research Site
67033 Strasbourg
France

Status: Rekrutierend

Research Site
31059 Toulouse cedex 9
France

Status: Rekrutierend

Research Site
54511 Vandoeuvre les Nancy Cedex
France

Status: Rekrutierend

Research Site
12200 Berlin
(Berlin)
Germany

Status: Rekrutierend

Research Site
01307 Dresden
(Sachsen)
Germany

Status: Rekrutierend

Research Site
20246 Hamburg
(Hamburg)
Germany

Status: Rekrutierend

Research Site
50924 Köln
(Nordrhein-Westfalen)
Germany

Status: Rekrutierend

Research Site
55131 Mainz
(Rheinland-Pfalz)
Germany

Status: Rekrutierend

Research Site
68100 Alexandroupoli
Greece

Status: Rekrutierend

Research Site
10676 Athens
Greece

Status: Rekrutierend

Research Site
115 22 Athens
Greece

Status: Rekrutierend

Research Site
11525 Athens
Greece

Status: Rekrutierend

Research Site
11528 Athens
Greece

Status: Rekrutierend

Research Site
18547 Athens
Greece

Status: Rekrutierend

Research Site
26504 Patra
Greece

Status: Rekrutierend

Research Site
54007 Thessaloniki
Greece

Status: Rekrutierend

Research Site
57010 Thessaloniki
Greece

Status: Rekrutierend

Research Site
467-8602 Nagoya-shi
Japan

Status: Rekrutierend

Research Site

441-8570 Toyohashi-shi
Japan

Status: Rekrutierend

Research Site
296-8602 Kamogawa-shi
Japan

Status: Rekrutierend

Research Site
811-1395 Fukuoka-shi
Japan

Status: Rekrutierend

Research Site
503-8502 Ogaki-shi
Japan

Status: Rekrutierend

Research Site
377-0280 Shibukawa-shi
Japan

Status: Rekrutierend

Research Site
670-8540 Himeji-shi
Japan

Status: Rekrutierend

Research Site
663-8501 Nishinomiya-shi
Japan

Status: Rekrutierend

Research Site
317-0077 Hitachi-shi

Japan

Status: Rekrutierend

Research Site
602-8566 Kyoto-shi
Japan

Status: Rekrutierend

Research Site
983-8520 Sendai-shi
Japan

Status: Rekrutierend

Research Site
951-8566 Niigata-shi
Japan

Status: Rekrutierend

Research Site
701-1192 Okayama-shi
Japan

Status: Rekrutierend

Research Site
543-8555 Osaka-shi
Japan

Status: Rekrutierend

Research Site
589-8511 Osakasayama-shi
Japan

Status: Rekrutierend

Research Site
565-0871 Suita-shi
Japan

Status: Rekrutierend

Research Site
350-8550 Kawagoe-shi
Japan

Status: Rekrutierend

Research Site
320-0834 Utsunomiya-shi
Japan

Status: Abgeschlossen

Research Site
113-8431 Bunkyo-ku
Japan

Status: Rekrutierend

Research Site
135-8550 Koto-ku
Japan

Status: Rekrutierend

Research Site
150-8935 Shibuya-ku
Japan

Status: Rekrutierend

Research Site
50009 Kaunas
Lithuania

Status: Rekrutierend

Research Site

08661 Vilnius
Lithuania

Status: Rekrutierend

Research Site
1081 HV Amsterdam
Netherlands

Status: Rekrutierend

Research Site
7334 DZ Apeldoorn
Netherlands

Status: Rekrutierend

Research Site
2134 TM Hoofddorp
Netherlands

Status: Rekrutierend

Research Site
022328 Bucharest
Romania

Status: Rekrutierend

Research Site
030171 Bucharest
Romania

Status: Rekrutierend

Research Site
050098 Bucharest
Romania

Status: Rekrutierend

Research Site
020125 Bucuresti

Romania

Status: Rekrutierend

Research Site
400124 Cluj-Napoca
Romania

Status: Rekrutierend

Research Site
700483 Iasi
Romania

Status: Rekrutierend

Research Site
410469 Oradea
Romania

Status: Rekrutierend

Research Site
550245 Sibiu
Romania

Status: Rekrutierend

Research Site
300079 Timisoara
Romania

Status: Rekrutierend

Research Site
660022 Krasnoyarsk
Russian Federation

Status: Rekrutierend

Research Site
123182 Moscow
Russian Federation

Status: Rekrutierend

Research Site
125284 Moscow
Russian Federation

Status: Rekrutierend

Research Site
185019 Petrozavodsk
Russian Federation

Status: Rekrutierend

Research Site
197341 Saint Petersburg
Russian Federation

Status: Rekrutierend

Research Site
443079 Samara
Russian Federation

Status: Rekrutierend

Research Site
851 07 Bratislava
Slovakia

Status: Rekrutierend

Research Site
07010 Palma de Mallorca
Spain

Status: Rekrutierend

Research Site
37007 Salamanca
Spain

Status: Rekrutierend

Research Site
08916 Badalona
Spain

Status: Rekrutierend

Research Site
08036 Barcelona
Spain

Status: Rekrutierend

Research Site
28223 Pozuelo de Alarcon
Spain

Status: Rekrutierend

Research Site
31008 Pamplona
Spain

Status: Rekrutierend

Research Site
791 82 Falun
Sweden

Status: Rekrutierend

Research Site
413 45 Goteborg
Sweden

Status: Rekrutierend

Research Site
301 85 Halmstad
Sweden

Status: Abgeschlossen

Research Site

971 80 Lulea
Sweden

Status: Rekrutierend

Research Site
221 85 Lund
Sweden

Status: Rekrutierend

Research Site
06560 Ankara
Turkey

Status: Rekrutierend

Research Site
06590 Ankara
Turkey

Status: Rekrutierend

Research Site
34093 Istanbul
Turkey

Status: Rekrutierend

Research Site
34214 Istanbul
Turkey

Status: Rekrutierend

Research Site
34387 Istanbul
Turkey

Status: Rekrutierend

Research Site
35340 Izmir

Turkey

Status: Rekrutierend

Research Site
38039 Kayseri
Turkey

Status: Rekrutierend

Quelle: ClinicalTrials.gov