INTERIM RESULTS OF THE NON-INTERVENTIONAL STUDY CARO

CARFILZOMIB IN COMBINATION WITH LENALIDOMIDE AND DEXAMETHASONE OR CARFILZOMIB IN COMBINATION WITH DEXAMETHASONE ALONE IN PATIENTS WITH MULTIPLE MYELOMA WHO HAVE RECEIVED AT LEAST ONE PRIOR THERAPY

Knauf W[1],
Ammon A[2],
Uhlig J[3],
Merling, M[4],
Hurtz HJ5,
Vannier C[4],
Schulz H[6],
Marschner N[7],
Riedt T[4],
Potthoff K[4]

1 Centrum für Hämatologie und Onkologie Bethanien, Frankfurt a. M., Germany

2 OSP Göttingen, Göttingen, Germany

3 Praxis Dr. med. Jens Uhlig, Naunhof, Germany

4 iOMEDICO, Freiburg i. Br., Germany

5 Gemeinschaftspraxis für Innere Medizin, Hämatologie, Onkologie, Gastroenterologie, Halle (Saale), German

6 Praxis Internistischer Onkologie und Hämatologie (PIOH), Frechen, Germany

7 Praxis für interdisziplinäre Onkologie & Hämatologie, Freiburg, Germany

INTRODUCTION

Poor adherence to antineoplastic treatment is a serious issue in the management of cancer patients since non-adherence has been shown to lead to higher treatment failure rates, worse outcome and higher total costs of care. The combination of the proteasome inhibitor carfilzomib (Kyprolis®) with lenalidomide (Revlimid®) and dexamethasone (KRd) or with dexamethasone alone (Kd) is approved for the treatment of patients with multiple myeloma who have received at least one prior therapy. Data from the pivotal phase III studies leading to approval of both regimens showed that carfilzomib therapy extended the median overall survival (mOS) (ASPIRE: mOS 48.3 months for KRd vs. 40.4 months for Rd, HR=0.79, p=0.0045[1]; ENDEAVOR: mOS 47.6 months for Kd vs. 40.0 months for bortezomib and dexamethasone, HR=0.79, p=0.010[2]) and improved health-related quality of life[3,4]. According to the current approved schedule, carfilzomib has to be given twice-weekly in both dose regimens (KRd, Kd)[5]. Real-world data on the implementation of this treatment recommendation and patients' adherence to the schedule prescribed by the treating physician are limited.

CONCLUSION

At the time of interim analysis, the mean total adherence to the prescribed carfilzomib dosing regimen in patients treated with KRd was almost 95% with nearly 90% of patients having an adherence rate of >90%. The implementation of the recommended twice-weekly approved KRd dosing schedule was 86% concerning number and timing of carfilzomib administrations and more than 90% concerning dosing of carfilzomib with a relative mean dose intensity of 88.1%.

Though, despite the required twice-weekly dosing schedule, the carfilzomib dosing regimen seems to be a convenient and feasible treatment option for multiple myeloma patients. Results have to be confirmed at final analysis.

METHODS

The prospective, multicenter, observational CARO study is designed to collect data on 300 patients with multiple myeloma (KRd: 200, Kd: 100) from 90 sites across Germany.

Primary objective is to assess patients' adherence to carfilzomib therapy (i.e., the extent to which a patient's actual administered medication corresponds to the prescribed medication; refer to **Figure 1**). Secondary objectives are patients' adherence to lenalidomide and dexamethasone as well as the real-world implementation of the recommended KRd or Kd dosing regimens (i.e., the extent to which the actual administered medication corresponds to the recommended medication according to current Summary of Product Characteristics (SmPC)); refer to **Figure 1**) in clinical routine. Exploratory objectives are effectiveness, safety and health-related quality of life. The first interim analysis of the CARO study was scheduled to assess the primary and secondary endpoints 12 months after the recruitment of the first patient.

RESULTS

From October 2016 to October 2017, 102 patients had been enrolled at 46 sites across Germany. Thereof 68 patients were assigned to the KRd cohort and 32 patients to the Kd cohort. Here, data with focus on adherence from patients with documented KRd therapy (N=64) at the time of the pre-specified interim analysis (database cut: 25 October 2017) are shown. Baseline patient characteristics are depicted in **Table 1**.

The mean total adherence to the carfilzomib dosing regimen, i.e. the extent of carfilzomib doses (with regard to number of applications, timing and dosage) administered as prescribed by the treating physicians and not modified due to adherence reasons, was 94.8% (total adherence, all cycles). In terms of timing, adherence was 99.4%. Adherence concerning number of applications and dosage were 98.4% and 96.6%, respectively (all cycles). In later cycles adherence was higher (**Table 2**).

89.1% of patients (n=57) had a total adherence rate of >90% to carfilzomib (all cycles) (**Figure 2**). Adherence to timing of >90% (all cycles) was observed in 98.4% of patients (n=63). 95.3% (n=61) and 93.8% (n=60) of patients, respectively, had an adherence rate of >90% concerning dosage and number of carfilzomib applications (all cycles). In later cycles adherence rates of >90% were observed more frequently (**Table 3**). Total adherence rates of >90% to lenalidomide and dexamethasone were observed in 86.0% and 51.9% of patients, respectively (**Figures 3, 4**).

The recommended carfilzomib dosing regimen according to SmPC was well implemented with 86.0% of administrations given in time and 90.6% of administrations given at the recommended dose, resulting in a relative mean dose intensity of 88.1% (StD: 24.8%).

Figure 1

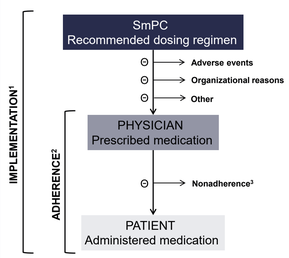

Figure 1
Implementation of SmPC and patients' adherence

[1]Extent to which patient's actual administered medication corresponds to the recommended medication according to current Summary of Product Characteristics (SmPC); [2]Extent to which patient's actual administered medication corresponds to the prescribed medication; [3]Predefined reasons for nonadherence to carfilzomib are: Patient did not appear as scheduled, Patient asked for delay/ modified schedule/ therapy break

Figure 2

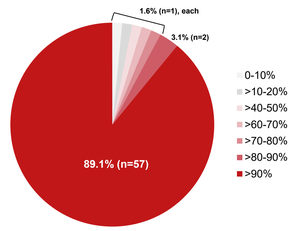

Figure 2
Percentage of patients with indicated total adherence rates to prescribed carfilzomib dosing regimen (N=64)

Figure 3

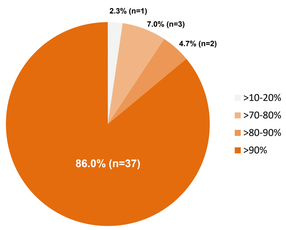

Figure 3
Percentage of patients with indicated total adherence to prescribed lenalidomide dosing regimen (N=43)

Figure 4

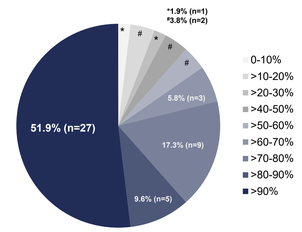

Figure 4
Percentage of patients with indicated total adherence to prescribed dexamethasone dosing regimen (N=52)

Table 1

Characteristic	FAS (N=64)
Age at date of informed consent, years	
Median	72.3
Range	43.4 – 84.3
Gender, n (%)	
Female	29 (45.3)
Male	35 (54.7)
Ethnicity, n (%)	
Caucasian	62 (96.9)
Other/Unknown	2 (3.1)
Karnofsky Performance Status, n (%)	
80-100	45 (70.3)
≤70	16 (25.0)
Missing	3 (4.7)

Table 1
Basic demographics

Table 2

	All cycles (N=64)	Cycles 1-3 (N=64)	Cycles 4-6 (N=35)	Cycles 7-9 (N=14)
Adherence to carfilzomib, mean [%] (Standard deviation)				
Total	94.8 (18.0)	95.2 (17.9)	97.3 (10.2)	100.0 (0.0)
Number of applications	98.4 (5.9)	98.7 (5.7)	98.7 (7.5)	100.0 (0.0)
Timing	99.4 (2.3)	99.6 (2.3)	98.3 (5.5)	100.0 (0.0)
Dosage	96.6 (16.0)	96.6 (16.0)	100.0 (0.0)	100.0 (0.0)

Table 2
Adherence to carfilzomib

Table 3

	All cycles (N=64)	Cycles 1-3 (N=64)	Cycles 4-6 (N=35)	Cycles 7-9 (N=14)
Patients with >90% adherence to carfilzomib, n (%)				
Total	57 (89.1)	58 (90.6)	33 (94.3)	14 (100.0)
Number of applications	60 (93.8)	60 (93.8)	34 (97.1)	14 (100.0)
Timing	63 (98.4)	63 (98.4)	33 (94.3)	14 (100.0)
Dosage	61 (95.3)	61 (95.3)	35 (100.0)	14 (100.0)

Table 3
Number of patients with an adherence rate >90% to carfilzomib

Abbrevations:
FAS: Full Analysis Set | Kd: Carfilzomib/dexamethasone | KRd: Carfilzomib/Lenalidomide/dexamethasone | mOS: median Overall Survival | SmPC: Summary of Product Characteristics | StD: Standard Deviation

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Conflicts of Interest:
Knauf, W.: Advisory Role or Expert Testimony: AMGEN GmbH, Honoraria: Amgen GmbH

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