AGMT_MM-2

A randomized Phase II, 2-armed study in transplant ineligible patients with newly diagnosed multiple myeloma (NDMM) comparing Carfilzomib + Thalidomide + Dexamethasone (KTd) versus Carfilzomib + Lenalidomide + Dexamethasone (KRd) induction therapy with respect to response rates and investigating a Carfilzomib (K) monotherapy maintenance strategy

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Study Rationale

KRd and KTd have been established as effective first line treatment protocols. In previous studies KRd was administered in the original twice weekly schedule, while in the present study carfilzomib will be infused once weekly (with a dose of 56 mg/m²). In addition to investigating the activity and tolerance of the once weekly carfilzomib regimen, the study will evaluate whether KTd will be non-inferior to KRd. The later regimen incorporates thalidomide, which is still widely used in Europe and all other regions outside US, while the former employs lenalidomide, an IMiD which is much more widely used in the US.

Protocol Synopsis

Indication: Newly diagnosed, transplant ineligible multiple myeloma (NDMM)

Study design: This is an international, multicenter, randomized, 2-arm phase II study

Planned sample size: 146 patients

Recruitment: 36 months

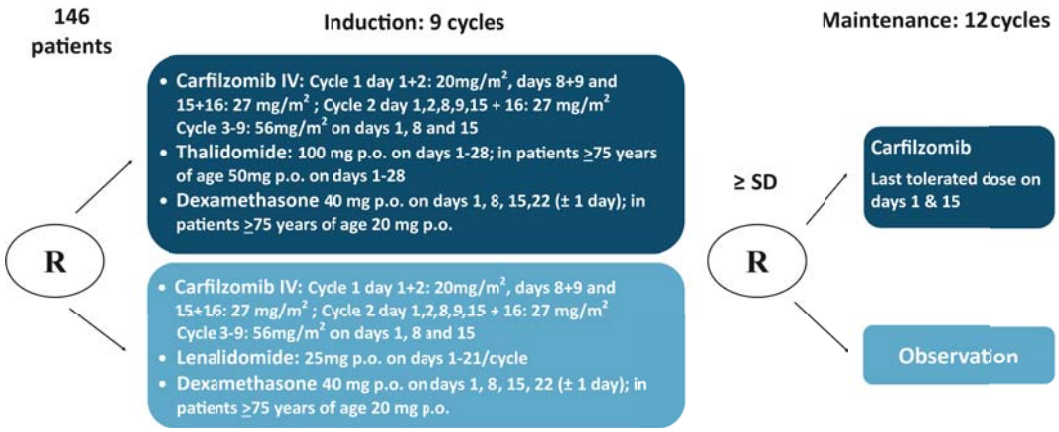
Duration: First patient in (FPI): Q1 2017
Last patient last visit (LPLV): 7 years after inclusion of first patient

Study medication: Carfilzomib

Primary objective:
To show non-inferiority with respect to response rates between KTd and KRd in patients after receiving 9 cycles induction therapy with either carfilzomib in combination with thalidomide and dexamethasone or carfilzomib in combination with lenalidomide and dexamethasone

Secondary objectives:
- Feasibility, safety and efficacy of a carfilzomib (K) maintenance therapy
- Response (PR, VGPR, CR, sCR, MRD according to IMWG)
- OS, safety and tolerability of patients receiving either KTd vs. KRd induction therapy and subsequent maintenance therapy
- PFS of both induction arms
- Quality of Life

Study Design



This is a randomized, 2-arm phase II, multicenter study to evaluate overall response rates and several other parameters in newly diagnosed, transplant ineligible patients receiving 9 cycles induction therapy with either KTd or KRd followed by randomization to either carfilzomib maintenance treatment or observation only. Maintenance is given for 12 cycles or progression of disease, whatever occurs first.

After 4 cycles stem cells can be harvested (optional) in those patients who may undergo autologous stem cell transplantation as salvage therapy.

Follow-up visits after completion of maintenance period will be performed in 3-monthly intervals until progression of disease or death.

Recruitment (Status as of March 2019): 67 patients

No	Site	Initiation	Patients
01	Wilhelminenspital / 1. Medizin	10.03.2017	8
02	PMU Salzburg / Innere Medizin III	22.03.2017	14
03	UK Graz / Innere Medizin - Hämatologie	12.04.2017	9
04	LKH Hochsteiermark / Dep. Hämato-Onkologie	10.03.2017	4
05	LKH Steyr / Innere Medizin II	30.05.2017	6
06	Kepler UK, Med Campus III. / UK Hämatologie	21.03.2017	3
07 + 08	Ordensklinikum Linz / Interne I	15.03.2017	3
09	AKH MUW / Innere Medizin I - Onkologie	21.04.2017	0
10	AKH MUW / Innere Medizin I - Hämatologie	12.04.2017	1

No	Site	Initiation	Patients
11	KH St. Vinzenz Zams / Innere Medizin	21.04.2017	4
12	UK Innsbruck / Innere Medizin V	21.04.2017	5
13	BKH Kufstein / Interne II	21.04.2017	1
14	SMZ Ost / 2. Medizin	31.01.2018	2
15	LKH Feldkirch / Innere Medizin II - Interne E	14.03.2017	4
16	UK Krems / Innere Medizin II	28.04.2017	3
17	UK Leipzig	23.10.2018	0
18	UK Würzburg	17.12.2018	0
21	Hanusch KH / 3. Medizin	25.02.2019	0

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