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

Protocol Number: AGMT_MM-2
EudraCT Number: 2016-000475-24

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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/m^2). 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, while the former employs lenalidomide, an IMiD which is much more widely used in the US.

Based on data from Biran et al. (ASH 2016), increased frequencies of cardiac complications and thrombotic microangiopathy were seen in elderly patients receiving 70 mg/m^2 carfilzomib in combination with dexamethasone and lenalidomide. These findings led us to modify the protocol and to implement a run in phase with two conventionally dosed cycles before continuing with a once weekly dose of 56mg/m^2 . We have summarized these changes in an amendment to the protocol.

Study Synopsis:

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

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

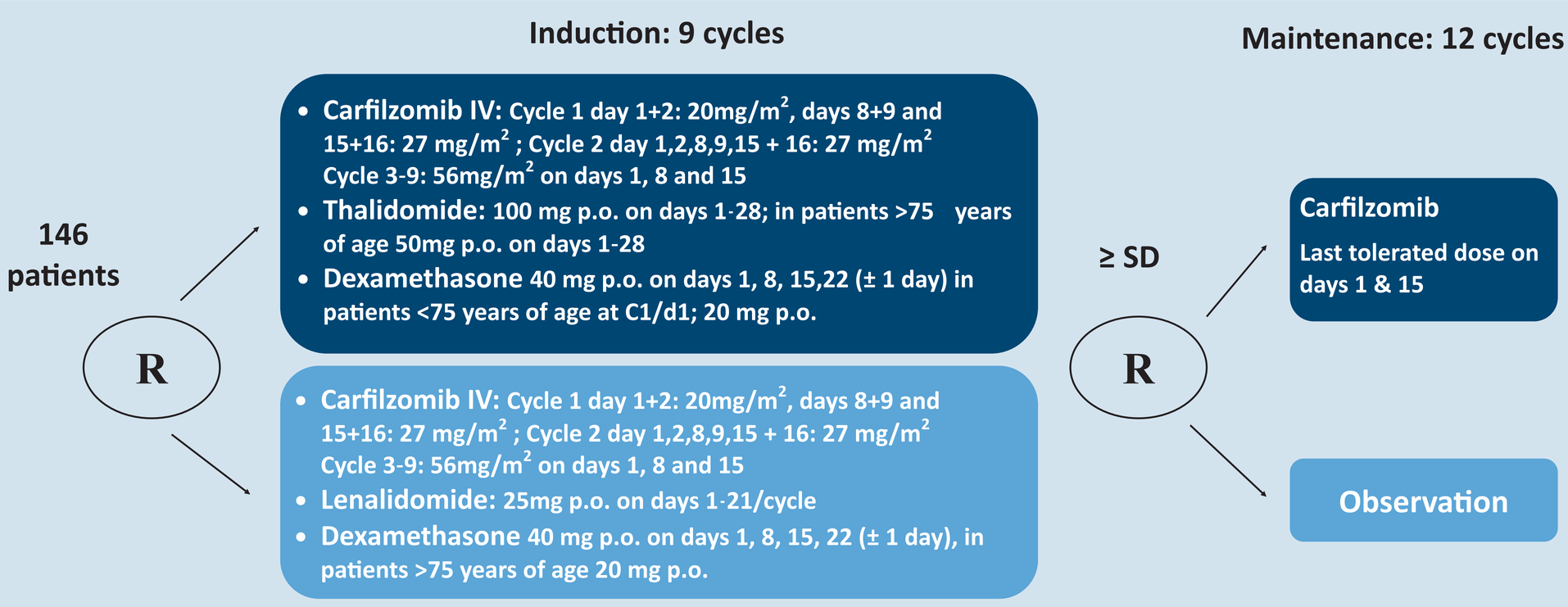
Primary objective:

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 K monotherapy maintenance
- Response (PR, VGPR, CR, sCR, MDR 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, multi-center 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.

Recruitment (Status as of March 2017):

The first two patients could be successfully enclosed to the study (PMU Salzburg, LKH Feldkirch).

An academic clinical trial
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