Ixazomib in Combination with Thalidomide – Dexamethasone in patients with relapsed and/or refractory multiple myeloma

Protocol Number: AGMT_MM-1 / EMN-13
EudraCT Number: 2014-002749-23
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Study Rationale:

Ixazomib in combination with Revlimid and Dexamethasone was significantly superior to Revlimid and Dexamethasone in relapsed patients after 1-3 prior treatment lines. Thalidomide has been shown to be equipotent to Revlimid in combination with alkylators or Bortezomib. Here, we explore the efficacy and tolerance of an oral combination regimen utilizing Ixazomib, Thalidomide and Dexamethasone.

Protocol Synopsis:

Indication: relapsed and/or refractory multiple myeloma

Study design: This is an open phase II, single-arm, multi-center and multinational study with sites in Austria, Germany and Czech Republic.

Planned sample size: 77 evaluable patients (≥ 2 cylces completed)

Recruitment: 24 months

Duration:
First patient in (FPI): Q2 2015
Last patient in (LPI): Q2 2017 (expected)
Last patient out (LPO): Q3 2019 (expected)

Study medication: Ixazomib

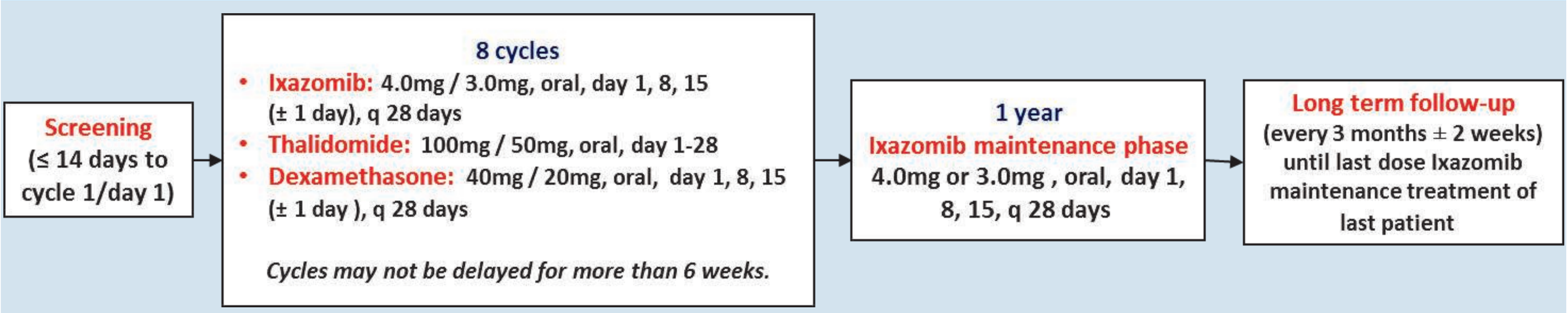
Primary objective:

- The primary endpoint is progression free survival (PFS)

Secondary objectives:

- Overall Response Rate (ORR), Overall Survival (OS)
- Safety profile of combination and maintenance treatment
- Quality of Life
- Association of PFS, OS, ORR with risk factors at diagnosis (e.g. clinical assessments, lab values and cytogenetic abnormalities)
- Association of possible correlations between altered expressions of specifically selected genes and their response to the treatment regimen

Study Design:



A safety analysis was conducted after enrolment of the first 6 patients who had completed at least two cycles or who had to stop treatment prematurely due to unacceptable toxicity. Data showed toxicities within the expected scope and did not enhance any consequences for the further conduct of the study.

Inclusion Criteria (selected):

- Male or female patients 18 years or older
- Patients in need of therapy with a diagnosis of relapsed or refractory multiple myeloma who had at least one prior treatment line (induction + autologous SCT + consolidation + maintenance therapy = 1 therapy line)
- Patients must have measurable disease defined by at least 1 of the following criteria:
  - Serum M-protein ≥ 10g/l
  - Urine M-protein ≥ 200mg/24h
  - Serum free light chain assay: involved serum light chain ≥ 10mg/dl provided that free light chain ration is abnormal
- ECOG ≤ 2
- Disease free of prior malignancies for ≥ 2 years with exception of curatively treated basal cell, squamous cell carcinoma of the skin, or carcinoma “in situ” of the cervix or breast
- Male and female: adaequate contraception if not post-menopausal
- Adequate hematology, liver and renal function

Recruitment (Status as of March 2017):

No	Site	Initiation	Patients
01	Wilhelminenspital Wien	05.05.2015	11
02	LKH Salzburg, Univ. Klinikum der PMU	14.04.2015	7
03	KH der Barmherzigen Schwestern Linz	24.08.2015	4
04	Klinikum Wels-Grieskirchen	28.04.2015	1
05	AKH Linz	22.04.2015	4
06	KH der Elisabethinen Linz	20.07.2015	7
07	Med. Universität / AKH Wien	09.04.2015	1
08	Universitätsklinik Innsbruck	26.05.2015	5
09	KH der Barmherzigen Brüder Wien	09.06.2015	0
10	LKH Feldkirch	14.12.2015	2
11	Bezirkskrankenhaus Kufstein	13.06.2016	1
12	Universitätsklinik Graz	07.04.2016	2
13	Universitätsklinikum Leipzig	24.03.2016	10
14	Universitätsklinik Tübingen	07.04.2016	3
15	Universitätsklinik Würzburg	17.03.2016	7
16	Faculty Hospital MU Brno	10.08.2016	2
17	Fakultní nemocnice Ostrava	13.06.2016	7
	Total	*7 patients terminated early	**74***

An academic clinical trial
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