# Clinical trials with recruitment





## **Clinical trials with recruitment**

Dg.		Title	Arms
MM	R/R	Panorama 3	Panobinostat, Bortezomib, Dexamethasone
		AGMT – EMN-13	Ixazomib, Thalidomid, Dexamethasone
		PCYC-1138	Ibrutinib, Pomalidomid, Dexamethasone
		PCYC-1139	Ibrutinib, Velcade, Dexamethasone
		EMN11/HO114	Carfilzomib, Pomalidomide, Dexamethasone
		CA209-602	Nivolumab, Elotuzumab, Pomalidomide, Dexamethasone
	MT	C16021	MLN9708 vs. placebo



## Multiple myeloma

**New diagnosis** 

C16021 - UT

Relapsed

PCYC-1138-CA

CLBH589D2222 (Panorama3)

**PCYC-1139-CA** 

AGMT\_MM-1/EMN-13

CA209-602

EMN11/HO114 only for patients of

EMN02 study



## C16021

A Phase 3, Randomized, Placebo-Controlled, Double-Blind Study of Oral Ixazomib Maintenance Therapy After Initial Therapy in Patients With Newly Diagnosed Multiple Myeloma Not Treated With Stem Cell Transplantation.



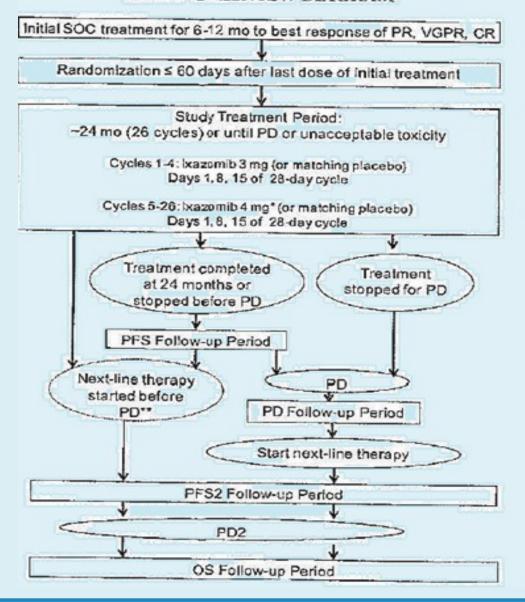
- completed 6 to 12 months of initial therapy with documented major response PR, VGPR, CR (maintained for 2 cycles after the M-protein nadir is reached)
- not eligible for ASCT
- ECOG 0-2

- relapsed/not responsive MM to initial therapy
- prior stem-cell transplantation
- radiotherapy within 14 days before randomization
- Diagnosis of Waldenstrom's macroglobulinemia, POEMS



## Study design

#### STUDY OVERVIEW DIAGRAM





## **PCYC-1138-CA**

A Randomized Multicenter Study of Ibrutinib in Combination with Pomalidomide and Dexamethasone in Subjects with Relapsed/Refractory Multiple Myeloma.

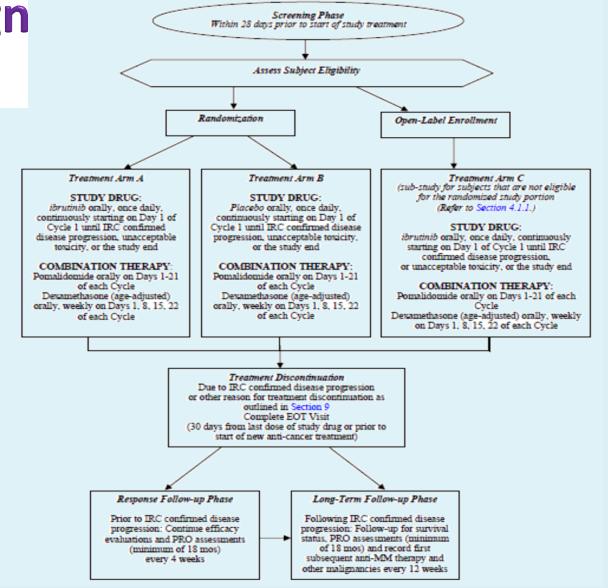


- relabující MM
- refrakterní MM
- nejméně 2 předchozí linie léčby
   MM včetně LEN a buď léčba
   s Bortezomibem nebo CFZ
- PD na léčbě nebo do 60 dní od ukončení léčby
- ECOG max. 2

- primárně refrakterní onemocnění
- předchozí léčba Pomalidomidem (výjma ramene C), BTK inhibitory
- syndrom POEM
- periferní neuropatie 2 a vyšší grade
- signifikantní GIT onemocnění



# Study Design of study 2b





## CLBH589D2222 (Panorama3)

A multicenter, randomized, open-label Phase 2 study evaluating the safety and efficacy of three different regimens of oral panobinostat in combination with subcutaneous bortezomib and oral dexamethasone in patients with relapsed or relapsed/refractory multiple myeloma who have been previously exposed to immunomodulatory agents.



- relapsed or relapsed and refractory mM
- 1-3 prior lines of therapy
- measurable disease
- ECOG 0-2
- prior IMiD exposure
- laboratory values within normal range

- primary refractory MM
- refractory to bortezomib
- prior treatment with DAC inhibitors including Panobinostat
- diarhea grade 2 and higher
- gastrointestinal dysfunction



## Study design

### Screening

#### Randomizace

Arm A: **PAN 20 mg TIW** (D 1, 3, 5, 8, 10, 12)

**BTZ**: C1-C4: ≤ 75 years: BTZ:1.3 mg/m2 (D1, 4, 8 & 11); > 75 yrs OW (D1, 8)

C5+: BTZ 1.3mg/m2 QW (D1,8)

Dexa: 20 mg/day for patients ≤
75years of age on 1st day of
screening; 10 mg/d for patients >
75 years of age on 1st day of
screening; On the day of BTZ
treatment (about 15 − 30
minutes prior to BTZ s.c.
injection) and the day after BTZ

Arm B: **PAN 20 mg BIW** (D 1, 4, 8, 11)

**BTZ**: C1-C4: ≤ 75 years: BTZ:1.3 mg/m2 (D1, 4, 8 & 11); > 75 yrs OW (D1, 8)

C5+: BTZ 1.3mg/m2 QW (D1,8) **Dexa**: 20 mg/day for patients ≤
75years of age on 1st day of
screening; 10 mg/d for patients
> 75 years of age on 1st day of
screening; On the day of BTZ
treatment (about 15 – 30
minutes prior to BTZ s.c.
injection) and the day after BTZ
treatment.

Arm A: **PAN 10 mg TIW** (D 1, 3, 5, 8, 10, 12)

**BTZ**: C1-C4: ≤ 75 years: BTZ:1.3 mg/m2 (D1, 4, 8 & 11); > 75 yrs OW (D1, 8)

OW (D1, 8)
C5+: BTZ 1.3mg/m2 QW (D1,8) **Dexa**: 20 mg/day for patients ≤
75 years of age on 1st day of
screening; 10 mg/d for patients >
75 years of age on 1st day of
screening; On the day of BTZ
treatment (about 15 − 30
minutes prior to BTZ s.c.
injection) and the day after BTZ
treatment.

### Follow-up

prior PD – every 6 weeks post PD – every 12 weeks



treatment.

## **PCYC-1139-CA**

An Open-label study of Ibrutinib in Combination with Bortezomib and Dexamethasone in Subjects with Relapsed or Relapsed and Refractory Multiple Myeloma.



- relapsed MM or relapsed and refraktory MM
- prior bortezomib exposure
- received 1-3 prior lines of therapy with demonstrated PD since completion of the most recent treatment regiment
- SPEP more than 1 g/dL lgG, others more than 0.5 g/dL
- ECOG max. 2

- primary refraktory disease
- prior exposure to BTK inhibitors
- syndrom POEM
- prior allogeneic cell transplant
- peripheralneuropathy grade 2 or higher



## Study Design

#### SCREENING

Within 30 days prior to start of study treatment (Refer to Section 8.2 for details of required assessments)

#### ASSESS ELIGIBILITY/ENROLLMENT

If subject satisfies all inclusion/exclusion criteria, following review of eligibility and confirmation of enrollment from Sponsor, initiate study treatment

#### Treatment Cycles 1-8 (21-day cycle)

#### STUDY TREATMENT:

Ibrutinib 840 mg orally, once daily continuously starting Day 1 of Cycle 1 until confirmed PD, unacceptable toxicity or other protocol specified reason for discontinuation COMBINATION THERAPY:

Bortezomib 1.3 mg/m<sup>2</sup> SC on Days 1, 4, 8 and 11 of each Cycle Dexamethasone 20 mg orally on Days 1,2,4,5,8,9,11 and 12 of each Cycle

#### Treatment Cycles 9-12 (42-day cycle)

#### STUDY TREATMENT:

Ibrutinib 840 mg orally, once daily continuously until confirmed PD, unacceptable toxicity or other protocol specified reason for discontinuation COMBINATION THERAPY:

Bortezomib 1.3 mg/m<sup>2</sup> SC on Days 1, 8, 22 and 29 of each Cycle Dexamethasone 20 mg orally on Days 1,2,8,9,22,23,29 and 30 of each Cycle

#### Treatment Cycles 13+ (28-day cycle)

#### STUDY TREATMENT:

Ibrutinib orally 840 mg, once daily continuously until confirmed PD, unacceptable toxicity or other protocol specified reason for discontinuation COMBINATION THERAPY:

Dexamethasone 40 mg orally once weekly

#### TREATMENT DISCONTINUATION

Due to confirmed PD, unacceptable toxicity or other reason for treatment discontinuation (Refer to Section 9.2). Complete EOT visit.

#### Response Follow-up

Prior to confirmed PD. Continue efficacy evaluations every 4 weeks until confirmed PD.

#### Long-Term Follow-up

Following confirmed PD. Follow-up for survival status and record first two subsequent anti-MM therapies and other malignancies every 12 weeks.



## AGMT\_MM-1/EMN-13

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



- relapsed or refractory MM
- at least 1 prior line of therapy
- measurable disease
- GFR nad 15 ml/min (MDRD)
- ECOG max. 2

- previous treatment with bortezomib nebo thalidomide within the last 3 months prior to baseline visit
- primary refractory MM
- prior treatment with Ixazomib
- neuropathy 3 and higher



## **Study Design**

Screening (≤ 14 days to cycle 1/day 1)

8 cycles à 28 days:

Ixazomib 4.0mg po on days 1, 8, 15 (± 1 day)

 Thalidomide 100mg po on days 1-28 in patients <75 years of age at C1/d1 50mg po on days 1-28 in patients ≥ 75 years of age at C1/d1

Dexamethasone 40mg po on days 1, 8, 15 (± 1 day )in patients <75 years of age at C1/d1</li>

20mg po on days 1, 8, 15 (± 1 day) in patients ≥ 75 years of age at C1/d1

Cycles may not be delayed for more than 6 weeks.

End of ITD treatment visit (= Start of Ixazomib maintenance phase)
(within 14 days after <u>last dose</u> (= D28) of last combination treatment cycle)

In case a patient is not enrolled in the maintenance phase due to response ≤SD after 4 cycles, PD, patient's or investigator's decision, he/she will enter the follow-up phase until end of the study

(4.0mg/3.0mg\*) po on days 1, 8, 15 every 28 days for a maximum duration of 12 months

End of Ixazomib maintenance phase (14 ± 7 days after last ixazomib dose)

Long term follow-up (every 3 months ± 2 weeks) until last dose ixazomib maintenance treatment of last patient

\*) 4.0mg in patients <75 years of age, 3.0mg in patients ≥ 75 years of age at start of maintenance phase



## CA209-602

An Open-Label, Randomized Phase 3 Trial of Combinations of Nivolumab, Elotuzumab, Pomalidomide and Dexamethasone in Relapsed and Refractory Multiple Myeloma.



- "double refractory" = refractory to PI and IMID or "relapsed nad refractory" = previous treatment with PI or IMID, or both, but Pdwithin 6 months, and refractory to theri last treatment
- measurable disease
- 2 or more prior lines with IMID and PI

- solitary bone or extramedullary plasmocytoma as the only evidence of plasma cell dyscrasia
- syndrome POEM
- prior exposure nivolumab, pomalidomide, elotuzumab
- NYHA III, IV



#### Arm A Nivolumab: Study Design Cycles 1 through 4: 240 mg IV Days 1, 15 of each 28 day Inv arm Cycles 5 and beyond: 480 mg IV Day 1 of each 28 day cycle 174 Pomalidomide: 4 mg po daily (Days 1-21) of each 28-days cycle. Dexamethasone: 40 mg pe per day (Days 1, 8, 15, 22) of each 28-days cycle for subjects \$ 75 years old. 20 mg po per day (Days 1, 8, 15, 22) of each 28-days cycle for subjects > 75 years old. Primary endpoints ORR PFS Arm B R Pomalidomide: Relapsed? 4 mg po daily (Days 1-21) of each 28-days cycle. A Refractory N myeloma D Control arm failed Dexamethasone: 0 proteasome 40 mg pe per day (Days 1, 8, 15, 22) of each 28-days cycle 174 м inhibitor and for subjects ≤ 75 years old. 20 mg po per day (Days 1, 8, 15, 22) of each 28-days cycle an IMiD z for subjects > 75 years old. A Cross-over upon progression 0 N\* Arm C Nivolumab: 3:3:1 Cycles 1 through 4: 240 mg IV Days 1, 15 of each 28 day Öycles 5 and beyond: 480 mg IV Day 1 of each 28 day cycle. Elotuzumab: 405 Cycles 1 & 2: 10mg/kg IV Days 1, 8, 15, 22 subjects Cycles 3 & 4: 10mg kg IV Days 1, 15 Cycles 5 and beyond: 20mg/kg IV Day 1. Exp arm Pomalidomide: 4 mg po daily (Days 1-21) of each 28-days cycle. Dexamethasone (weeks with Elotuzumab dosing): · 28 mg PO + 8 mg IV on days of eleturumah doning (subjects ≤ 75 years) 8 mg PO + 8 mg IV on days of elotazumab dosing (aubjects > 75 years) Dexamethasone (weeks without Elotuzumab dosing): 40 mg PO for subjects ≤ 75 years old.

20 mg PO for subjects > 75 years old.



## EMN011/H0114

Pomalidomide combined with Carfilzomib and Dexamethasone (PCd) for induction and consolidation followed by Pomalidomide combined with Dexamethason vs Pomalidomide maintenance for patients with Multiple Myeloma in progression after prior 1st line treatment with Lenalidomide and Bortezomib.

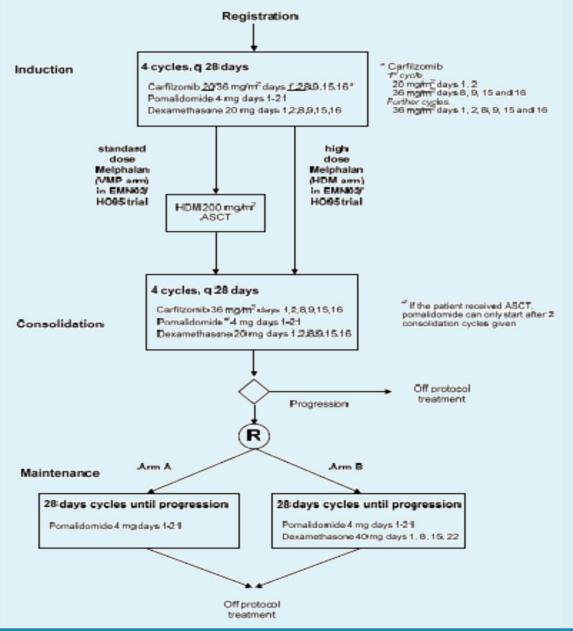


- included in EMN02 trial
- measurable disease
- documented PD or refractory
   MM as per IMWG criteria
- WHO 0, 1, 2

- recieved more than 1 line of therapy, except local radiotherapy
- syndrome POEM
- previous therapy with pomalidomide or carfilzomib
- LVEF no higher than 40 %
- NYHA III or IV



## **Study Design**





## Thank you.

